# South African Medical Journal

Organ of the Medical Association of South Africa

# S.-A. Tydskrif vir Geneeskunde

Vakblad van die Mediese Vereniging van Suid-Afrika

Incorporating the *South African Medical Record* and the *Medical Journal of South Africa*

REGISTERED AT THE GENERAL POST OFFICE AS A NEWSPAPER

Vol. 26, No. 5 | Cape Town, 2 February 1952 | Weekly 2s 6d


IN THIS ISSUE

South African Medical Journal
Suid-Afrikaanse Tydskrif vir Geneeskunde
P.O. Box 643, Cape Town Posbus 643, Kaapstad

Vol. 26, No. 5 Cape Town, 2 February 1952 Weekly 2s 6d

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# THE MEDICO-LEGAL PRECIPITIN TEST FOR HUMAN BLOOD*

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The fundamental principles of the precipitin test are based on serological animal studies. Nuttal [22] carried out precipitin tests on the bloods of an extensive range of animal species. He concluded that in general the reactions obtained in these experiments were proportional to the zoological relationship of the animal species, e.g. it was shown that the Old World monkeys are more closely allied to man than the New World monkeys.

In order to obtain specific serological reactions for testing animal bloods, several other serological tests have been used. Notably a complement deviation test (Uhlenhuth as quoted by Sutherland [31]), a modified agglutination test (Landsteiner and Miller [15]), a complement fixation test (Kolmer and Boerner [10]) and an 'inhibition test' (Wiener *et al.*[40]) are described. However, Landsteiner and van den Scheer [17] and Landsteiner and Miller [16] point out that lysins and agglutinins do not parallel the zoological relationships of the animal species to the extent which is apparent in precipitin reactions. Lysin and agglutinin antigens may show differences in related species and even in the same animal species, and yet may exhibit similarities in distantly related species.

Thus for many years a precipitin test has been employed for establishing that a blood stain is human. Various methods have been described for carrying out this test and for preparing suitable antisera. An analysis of most of these methods indicates that whereas the tests appear to exclude reactions with the bloods of unrelated animals, reactions with the sera of monkeys, baboons and anthropoid apes are nevertheless encountered. The reactions with these animals do not present special importance in certain countries. However, the exclusion of reactions with the bloods of these species is of considerable significance in Southern Africa. The greater proportion of exhibits submitted for medico-legal examination is obtained in cases of murder, rape, etc., affecting the non-European population, in particular the Bantu. In many of the rural areas of the country, e.g. Zululand, monkeys and 'bush babies' are killed with weapons such as 'assegais', which are also used in cases of assault. Likewise, in other parts of the country the exhibits are liable to contamination with baboon blood. Further the dried skins of these animals are frequently worn by the Bantu as clothes or ornaments.

For these reasons the adoption of some method which would serve to exclude with certainty the blood of monkeys, baboons, 'bush babies' and the 'Nachtaapje' is of considerable importance. Special attention, therefore, has been given to this problem in this paper.

The efficacy of the test is mainly dependent upon the preparation of a specific and potent anti-human precipitin serum.

## A REVIEW OF THE METHODS IN GENERAL USE FOR THE PREPARATION AND STANDARDIZATION OF ANTI-HUMAN PRECIPITIN SERA

The customary method as set out in most textbooks on Forensic Medicine is as follows: Rabbits are injected with ascending successive doses of human serum either by the subcutaneous, intravenous or intraperitoneal routes or the latter two combined (Sutherland [32], Lynch [19], Smith and Fiddes [26], Kolmer and Boerner [11], Taylor [34], Wiener [38], and Schiff and Boyd [25]). Antisera prepared in this way are then tested for potency by the end-point titre method of titration and varying standards have been laid down (Table I).

Several authors recommend that the anti-human precipitin sera should be tested for specificity. Here again different standards are indicated (Table II).

It is evident from an analysis of Tables I and II, that the standards acceptable to the various authors differ. Similarly, the exact conditions of titration are variable, e.g. the volume of the test, quantities of antibody and antigen, time allowed for precipitation, the pH of the medium and the temperature of the test. Consequently, a comparison of the standards is not practicable.

Wolfe [41] has shown that by the repeated injection method of immunization the potency of the antiserum is increased but the titre for the heterologous animal is proportionately increased to a greater degree than that for the homologous animal serum. Further the increase in titre is frequently greater with more distantly related animal bloods.

Proom [23] comments that in his experience antisera prepared by the technique of repeated intravenous and intraperitoneal injections usually lack specificity. He outlined a method for the production of various animal (not human) antisera. By using single intramuscular injections of alum-precipitated serum he was able to produce potent and highly specific antisera for the homologous animals. His criteria were as follows:

* This work was carried out at the Pathological Laboratory of the Union Health Department, Durban.

1. A definite reaction (ring formation) was produced with 1 : 8,000 dilution of the homologous serum.
2. No such reaction was produced with a 1 : 50 dilution of the sera of unrelated animal species.

This method has been applied to the production of anti-human precipitin sera for medico-legal purposes (Rhodes, Gordon and Turner [21]).

Nevertheless, I have found that although the antisera prepared by this method possess relatively high potency, reactions occur with the sera of other mammals. Nine separate antisera have been tested. Table III is an example of the results obtained. In no instance were reactions obtained against the sera of fish, frogs, snakes, rats or birds.

SOME METHODS EMPLOYED TO OBTAIN A SEROLOGICALLY SPECIFIC RESULT

1. THE END-POINT TITRE METHOD OF TITRATION

In the end-point titre method limiting dilutions of animal sera are tested against neat or a constant dilution of anti-human precipitin serum. The intensity of the reaction and the dilution of the antigen is greatest for the related animal species.

Reference to Table II shows that the authors have employed this technique as being indicative of specificity. Accordingly the methods for estimating the concentration of the antigen in the unknown blood stain are of impor-

TABLE I: STANDARDS OF POTENCY

| *Reference* | *Dilution of Antigen* | *Quantity of Antigen* | *Quantity of Neat Antibody* | *Grades of Reaction* | *Time for Testing* | *Temperature of the Test* | *Method Employed* |
|---|---|---|---|---|---|---|---|
| Sutherland (1907, c) | Human blood<br>1:1,000<br>1:10,000<br>1:20,000 | <br>20 parts<br>20 parts<br>20 parts | <br>1 part<br>1 part<br>1 part | <br>Precipitate<br>Precipitate<br>Precipitate | <br>2 minutes<br>3 minutes<br>5 minutes | <br>Room temperature<br>Room temperature<br>Room temperature | <br>Interfacial technique or ring test<br>Interfacial technique or ring test<br>Interfacial technique or ring test |
| Lynch (1928) .. | Human serum<br>1:5,000 | <br>— | <br>— | <br>Precipitate | <br>20 minutes | <br>Room temperature | <br>Interfacial technique or ring test |
| Lloyd as quoted by Lynch (1928) | 1:40,000 | — | — | Precipitate | — | Room temperature | Interfacial technique or ring test |
| Glaister (1945, a) .. | 1:20,000 | — | 1:10 the quantity of antigen | Distinct cloudiness | 20 minutes | Room temperature | Interfacial technique or ring test |
| Kolmer and Boerner (1945, c) | 1:1,000 | 1 cc. | 0·2 cc. | Precipitate | 5–15 minutes | Room temperature | Interfacial technique or ring test |
| Smith and Fiddes (1949, b) | 1:1,000<br>1:1,000 | —<br>— | 0·1 cc.<br>0·1 cc. | Turbidity<br>Precipitate | 5 minutes<br>30 minutes | Room temperature<br>Room temperature | Interfacial technique or ring test<br>Interfacial technique or ring test |
| Taylor (1948, a) .. | 1:10,000 | — | Few drops | Precipitate | 30 minutes | Room temperature | Interfacial technique or ring test |
| Uhlenhuth as quoted by Smith and Glaister (1939, a) | 1:1,000<br>1:1,000 | —<br>— | 0·1 cc.<br>0·1 cc. | Turbidity<br>Distinct Precipitate | Immediate or 1–5 minutes<br>30–60 minutes | Room temperature<br>Room temperature | Interfacial technique or ring test<br>Interfacial technique or ring test |
| * Schiff and Boyd (1942,) Boyd (1947, a) | 1:20,000 or over | — | — | Precipitate | 20 minutes | Room temperature | Interfacial technique or ring test |
| Wiener (1946, b) .. | 1:500<br>1:1,000<br>1:10,000 | 0·5 cc.<br>0·5 cc.<br>0·5 cc. | 0·1 cc.<br>0·1 cc.<br>0·1 cc. | Clouding<br>—<br>Turbidity | Immediate or 1–2 minutes<br>—<br>— | Room temperature<br>Room temperature<br>Room temperature | Tube Precipitation<br>Tube Precipitation<br>Tube Precipitation |

* The authors state that it is important to note the speed of the reaction, the amount of reaction and the density of the reaction.

TABLE II: STANDARDS OF SPECIFICITY

*Note:* No reaction, i.e. precipitation should occur in the following conditions of testing

| *Reference* | *Types of Animals to be excluded* | *Types of animal antigen* | *Dilution and/or quantity of antigen* | *Quantity of neat anti-human serum* | *Time for testing* | *Temperature of testing* | *Method employed* |
|---|---|---|---|---|---|---|---|
| Sutherland (1907, c) | All .. .. .. | Extract of animal bloods | 2 cc. | 0·1 cc. | 20 minutes | Room temperature | Interfacial technique |
| Lynch (1928) .. | All except closely related species | Animal serum | 1:100 or less | — | 20 minutes | Room temperature | Interfacial technique |
| Kolmer and Boerner (1945, c) | All. Doubt may arise with sera of higher apes | Animal serum | 1 cc. of a 1:1,000 dilution | 0·2 cc. | 5–15 minutes | Room temperature | Interfacial technique |
| Glaister (1945, b) .. | All .. .. .. | Blood | 1:1,000 | 1/10th the quantity of antigen | — | Room temperature | Interfacial technique |
| Taylor (1948, b) .. | All. Reactions with higher apes are good but less than with human blood. Slight reactions occur with monkey blood | Blood | 1:500—1:10,000 | Few drops | — | Room temperature | Interfacial technique |
| Smith and Fiddes (1949, b) | All. Reactions with the bloods of Anthropoid Apes are distinct but less than with human blood | Blood | 1:1,000 | — | Immediate | Room temperature | Interfacial technique |
| Wiener (1946, b) .. | All unrelated species | Serum | 0·5 cc. of a 1:100 and a 1:500 dilution | 0·1 cc. | 20 minutes | Room temperature | Tube precipitation |

TABLE III: TITRATIONS AGAINST LIMITING DILUTIONS OF MAMMALIAN SERA

METHOD EMPLOYED: INTERFACIAL TECHNIQUE. (PROOM[22])

| *Mammalian Species* | *Dilutions of Mammalian Sera* | | | | | |
|---|---|---|---|---|---|---|
| | 1:10 | 1:20 | 1:40 | 1:80 | 1:160 | 1:320 |
| "Bush Baby" .. | + | + | + | + | + | — |
| Ox .. .. | + | + | + | + | + | + |
| Horse .. .. | + | — | + | + | — | — |
| Sheep .. .. | + | — | + | — | — | — |
| Goat .. .. | + | + | — | — | — | — |
| Pig .. .. | + | + | + | + | + | — |
| Springbok .. | + | — | + | + | — | — |
| Dog .. .. | + | + | — | — | — | — |
| Cat .. .. | + | + | — | — | — | — |
| Rabbit .. .. | — | — | — | — | — | — |
| Guinea Pig .. | — | — | — | — | — | — |

A + sign denotes a zone of precipitation at the interfacial surface of the animal serum and the anti-human precipitin serum.

tance. Among the methods used are the foam test and the precipitation of the proteins with nitric or salicylsulphonic acid.

It would appear that the salicylsulphonic acid method (Lynch [13]) is the most satisfactory, but difficulties arise in the interpretation of the test. Smith and Glaister [29] comment that it is regrettable that there is no exact method for estimating the blood dilution in an extract of the unknown blood stain. The mucus of saliva or vaginal secretions is liable to be precipitated in acid solutions in the cold by the addition of salicylsulphonic acid. Similarly, animal proteins from the exhibit itself are liable to go into solution when steeped in saline, e.g. animal skins and hairs (the type of clothing often worn by the Bantu) and poorly processed woollen materials.

Topley and Wilson [36] point out that in the precipitin reaction the end-point titration method has limited application. There is no relationship expressed between the speed of the reaction and the relative concentrations of the antibody or the antigen. In addition the end-point tends to vary with small differences in the conditions under which the titrations are carried out. This is supported by Marrack [20] who states that the end-point titration in precipitin reactions where a constant antibody and limiting dilutions of antigen are used, is unsound. Further, two antisera may be of equal strength when titrated against one concentration of antigen, but may differ when another

TABLE IV: TITRATIONS OF ANTI-HUMAN PRECIPITIN SERA AGAINST LIMITING DILUTIONS OF PRIMATE SERA: TITRATION METHOD, INTERFACIAL TECHNIQUE (PROOM[23]). THE TITRATION RESULTS OF SIX SEPARATE NEAT ANTI-HUMAN PRECIPITIN SERA ARE RECORDED. WHERE A ZONE OF PRECIPITATION OCCURRED AT THE INTERFACIAL SURFACES THE REACTION IS RECORDED BY A NUMERAL CORRESPONDING TO THE ANTI-SERUM, VIZ. '1', '2', '3', '4', '5', AND '6'

| *Primate Species* | *Dilutions of Primate Sera* | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1:100 | | | 1:500 | | | 1:1,000 | | | 1:5,000 | | | 1:10,000 | | | 1:12,500 | | | 1:15,000 | | |
| Human | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 | 1 | | 3 | 1 | | 3 |
| | 4 | 5 | 6 | 4 | 5 | 6 | 4 | 5 | 6 | 4 | 5 | 6 | 4 | 5 | 6 | 4 | 5 | | | 5 | |
| Baboon | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 | | 2 | | | | |
| | 4 | 5 | 6 | 4 | 5 | | 4 | 5 | | 4 | 5 | | 4 | 5 | | 4 | 5 | | | 5 | |
| Monkey | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 | 1 | | 3 | 1 | | 3 | 1 | | | 1 | | |
| | 4 | 5 | 6 | 4 | 5 | 6 | 4 | 5 | | | 5 | | | 5 | | | 5 | | | 5 | |

Two further anti-human precipitin sera were titrated against the sera of various primate species, e.g. chimpanzee, Macacus rhesus, 2 species of baboon sera and 3 species of monkey sera. Reactions against these primate sera occurred in both instances in dilutions of at least 1:1,250 or more.

concentration of antigen is tested. The results are particularly liable to be affected by non-specific factors, such as the amount of non-antigenic serum protein present in the solution.

In addition I have obtained closely approximating end points of reaction when titrating anti-human precipitin sera (prepared according to the method of Proom [23]) against limiting dilutions of the sera of humans, monkeys and baboons. Table IV illustrates these findings.

### 2. The Optimal Proportions Method of Dean and Webb (1926) [5]

This method is a satisfactory means of detecting small quantities of a homologous antigen. The antigen and antibody are added in proportions most favourable to rapid precipitation. The result is not dependent upon a zone of reaction and the serological objections raised against the end-point titre method of titration in precipitin reactions are not encountered. This technique gains further support in that it has been used for the quantitative estimation of protein antigens (Taylor, Adair and Adair as quoted by Marrack [21]).

A further application of this method may be one of obtaining serological specificity. Dean, Taylor and Adair [4] have shown the following:

Rabbits were injected with two separate antigens—egg albumin and horse serum albumin. The antiserum showed two distinct precipitins each being specific in its reaction with the homologous antigen, even to the extent of nitrogen estimations.

It was proposed to apply this method to a quantitative estimation of the precipitinogens and thereby attempt to obtain a serologically specific result applicable to medico-legal work. Using six separate anti-human precipitin sera (prepared according to the method of Proom [23]), the antibody optimal proportion ratios for human, monkey and baboon sera were determined. It was found that the ratios in most cases approximated closely and, therefore, when used in testing the unknown medico-legal blood stain the results might be confusing.

### 3. Absorption Techniques

A further method for obtaining a serologically specific result is the absorption method of Weichert (Smith and Glaister [30]; Lynch [19]). In this method a heterologous antigen is added to the antiserum, the mixture is centrifuged and the supernatant fluid is used for testing. Fujiwara [6] by adding to the anti-human precipitin serum 10% by volume of Japanese ape serum, was able to obtain a more specific differentiation. Landsteiner and van den Scheer [18] have shown that after partial saturation of antisera with heterologous sera, the supernatants still contained antibodies which reacted with higher concentrations of the heterologous antigens. These latter experiments were carried out on anti-human precipitin sera and varying dilutions of Macacus rhesus sera were added for absorption.

Anti-human precipitin sera which I have prepared have followed an absorption technique: 7% by volume of ox serum has been added to the antisera. The mixtures were kept at room temperature for two hours and in the refrigerator (5° C.) overnight. The supernatants after centrifugation were used for medico-legal work. Titrations of these antisera have shown that ox absorption successfully removed the heterologous precipitins reacting with the sera of distantly related animal species, e.g. the sera of ox, horse, sheep, pig, springbok, dog, cat and guinea pig. Reactions were still encountered in high dilutions against the sera of various species of baboon and monkey and to a lesser extent against the sera of 'bush baby' and 'Nachtaapje'.

It is recommended by Boyd [2] that for the absorption of heterologous antibody the quantity of the heterologous antigen to be added to the antiserum should be that amount which will give rise to optimal flocculation (Dean and Webb [5]). This method has been used for the absorption of heterologous precipitinogens in six separate anti-human precipitin sera (prepared according to Proom [23]). The sera of the 'Somango' monkey and the 'Chacma' baboon were titrated and used for absorption. The resultant absorbed antisera were of a very low potency and despite further additions of the respective animal

sera, i.e. in excess of the optimal proportions ratio, reactions nevertheless occurred in low dilutions with heterologous primate sera. Further, these antisera were tested against unknown stains of various species of primate bloods and the results were most conflicting. The results of these absorption experiments compare with those reported by Proom [23] who tested various animal antisera.

#### 4. USE OF FRACTIONATED HUMAN SERA FOR IMMUNIZATION IN RABBITS

Fractionated human sera preparations have been used for immunizing rabbits. These antisera have been tested as previously described for the antisera prepared according to the method of Proom [23]. The results of the respective titrations have paralleled those described in the foregoing experiments. Two types of fractionated human sera have been investigated, viz. a total globulin preparation made by 50% ammonium sulphate fractionation and a gamma globulin preparation made according to the method of Kendal (Kabat and Mayer [9]). Electrophoretic analyses, however, of two of these globulin preparations showed that the methods employed were unsatisfactory. Both preparations were shown to contain considerable proportions of albumin. Nevertheless, the results of the titrations and absorption experiments of the antisera produced agree with the findings of Proom [23]. Proom showed that the titre and the specificity of anti-horse precipitin sera exhibited no appreciable differences when prepared by immunization with whole or fractionated horse serum. This is supported by Coombs and Mourant [3] in that for the purpose of detection of the sensitization of human red cells with 'incomplete' Rh antibody, immune sera prepared by the immunization of fractionated human sera preparations were not as satisfactory as those prepared by immunization with alum-precipitated whole sera.

Nevertheless, in view of the impure quality of the 'globulin' preparations I have used, it would appear that perhaps more recent methods of fractionation should be investigated and controlled electrophoretically before this method of immunization is overlooked.

#### 5. ANTI-HUMAN PRECIPITIN SERA PREPARED IN PRIMATES

Uhlenhuth's cross- immunization method is a further means of obtaining species specificity. Uhlenhuth [37] immunized monkeys with human blood and obtained antisera which reacted with human serum but showed no reaction when titrated against monkey serum. This work is supported by Landsteiner and Levine [14] in a similar experiment with chimpanzee. Landsteiner [13] considers that if antibodies are produced in the immunized animals they are either supressed or the process may be equivalent to an absorption *in vivo*.

Anti-human precipitin sera were prepared in two species of 'Vervet' monkeys, one species of 'Chacma' baboon and one species of 'Nachtaapje'. The immunization of the animals was carried out as follows:

(a) One species of 'Vervet' monkey and one species of 'Chacma' baboon were injected with alum-precipitated whole human serum (Proom [23]). Two injections were given at an interval of five days and the animals were bled 20 days after the last injection.

(b) One species of 'Vervet' monkey and one species of 'Nachtaapje' were immunized by an initial injection of alum-precipitated serum (Proom [23]), followed by three injections at five-day intervals of a globulin preparation made by 50%

TABLE V: TITRATIONS OF ANTI-HUMAN PRECIPITIN SERA PREPARED BY IMMUNISING PRIMATES
Method Employed: Interfacial Technique. (Proom 23)

| *Type of anti-human precipitin Serum* | *Primate Sera* | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *Human end-point titre of reaction* | *Chimpanzee dilution of serum* | | | *Baboon dilution of serum* | | | *Monkey dilution of serum* | | | *Galago dilution of serum* | | | |
| | | 1:5 | 1:10 | 1:20 | 1:5 | 1:10 | 1:20 | 1:5 | 1:10 | 1:20 | 1:5 | 1:10 | 1:20 | |
| Anti-human precipitin serum prepared in 'Chacma' baboon | 1:320 | + | + | + | — | — | — | — | — | — | — | — | — | |
| Anti-human precipitin serum prepared in 'Vervet' monkey (a) | 1:400 | + | + | + | — | — | — | — | — | — | + | — | — | |
| Anti-human precipitin serum prepared in 'Vervet' monkey (b) | 1:640 | End-point titre of reaction 1:320 | | | — | — | — | — | — | — | + | + | + | 1:40 + |
| | | *Dilution of serum* | | | | | | | | | | | | |
| | | 1:10 | 1:20 | 1:40 | 1:10 | 1:20 | 1:40 | 1:10 | 1:20 | 1:40 | 1:5 | | | |
| Anti-human precipitin serum prepared in 'Nachtaapje' | 1:320 | + | + | + | + | + | + | + | + | + | — | | | |

ammonium sulphate fractionation of fresh pooled human serum. Seven days after the last injection the animals were bled and the initial titrations showed a low potency antiserum. After 14 days the animals received three further injections at five-day intervals of fresh globulin preparations. The animals were finally bled 14 days after the last injection.

The injections of all the above human serum preparations were given intramuscularly in divided doses.

Titrations of these four antisera showed reactions in low dilutions against some of the mammalian sera, e.g. pig, dog and cat in dilutions 1:5 and 1:10. The end-point of titres of reaction against human serum and the reactions against other primate sera are shown in Table V.

## CONCLUSIONS

It would appear that in Southern Africa the precipitin test for human blood stains should entail the initial testing of the unknown blood stain extract against anti-human precipitin sera prepared in rabbits which has been treated by ox-absorption and then tested against a range of mammalian sera for specificity. In cases of suspected contamination of the stain with the bloods of any of the indigenous primates, the stain should then be tested against anti-human precipitin sera prepared in species of both Galago and Cercopithecidae (monkeys or baboons), to exclude these animal species.

## SUMMARY

1. The difficulties encountered in the carrying out of the precipitin test in Southern Africa are described.

2. The methods employed in the production of anti-human precipitin sera and the standards of potency and specificity are discussed.

3. Five lines of experimentation used to investigate the possibility of obtaining a serologically specific test are described.

4. A method of titrations recommended for Southern Africa is outlined.

This paper is published by kind permission of Dr. G. W. Gale, Secretary for Health, Union of South Africa. I wish to thank Prof. M. van den Ende and Dr. I. Gordon (Senior Government Pathologist, Durban) for their encouragement and guidance. I have to thank Prof. R. Turner and Dr. H. A. Shapiro for helpful suggestions and Dr. I. Prinsloo (Senior Assistant Government Pathologist, Durban), Dr. C. G. Anderson (South African Institute for Medical Research) and Mr. R. P. Nightingale for their assistance.

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## ABSTRACTS

*Thymidine and Vitamin $B_{12}$ in Pernicious Anaemia.* C. C. Ungley (1949): Lancet, **256**, 164.

A patient with Addisonian pernicious anaemia did not respond to thymidine but responded to a small dose of the red crystalline anti-pernicious-anaemia factor.

*Activity of Vitamin $B_{12}$ in Addisonian Pernicious Anaemia.* R. West (1948): Science, **107**, 398.

Doses of 3 to 15 micrograms crystalline Vitamin $B_{12}$ showed haematological activity in three cases of Addisonian pernicious anaemia.

South African Medical Journal
Suid-Afrikaanse Tydskrif vir Geneeskunde

## EDITORIAL

### THE PRECIPITIN TEST FOR HUMAN BLOOD

The field of forensic pathology is redolent of myth. Unverified allegations continue to be copied uncritically from textbook to textbook and are almost literally handed down from father to son. The province of serology is no exception to this rule, and major unwarranted assumptions about the specificity of the tests for human blood continue to be made. Modern serological techniques permit the revaluation of the adequacy of dogmas based on an inadequate appreciation of the limitations of the routine laboratory.

For these reasons the quantitative work reported by Dr. J. E. Duncan Taylor elsewhere in this issue has a special importance, particularly in South Africa, where the problems created by a possible confusion with non-human primate blood may be very real. Dr. Duncan Taylor's researches were carried out in Durban as a member of the staff of the Pathological Laboratory of the Union Health Department—a laboratory which has in recent times made distinguished contributions to medico-legal research.

The present issue is essentially a practical one because a decision affecting the life of an accused person may depend on the report of the forensic serologist, yet it is not generally appreciated that Man shares so closely with other primates a serological reaction to anti-human serum prepared in rabbits, that the test-tube reactions cannot be differentiated by the usual routine methods described in current medico-legal textbooks.

Dr. Duncan Taylor's work is a thorough survey of contemporary methods and demonstrates their inadequacy because of their non-specificity. The comprehensiveness of her research is reflected in the considerable range of animals tested, extending throughout all the phyla from fishes to birds.

One conclusion emerges clearly from her survey, viz. that there is no simple, practical method available for laboratory testing which can distinguish human blood stains from the blood stains of apes, monkeys (including baboons) or lemurs, e.g. the nagapie.

The medico-legal implications of this state of affairs are obviously very important. Her excellent investigation has made it clear that the greatest caution must be exercised in framing reports intended for our Courts so as not to create an impression that the tests have definitely proved a stain to be human. An expert witness who

## VAN DIE REDAKSIE

### DIE PRESIPITIENTOETS VIR MENSBLOED

Die sfeer van juridiese patologie wemel van fabelagtighede. Onbevestigde bewerings word voortdurend, sonder kritiek, van handboek na handboek oorgeskryf en word feitlik letterlik van vader tot seun oorgedra. Die gebied van serologie is geen uitsondering op hierdie reël nie, en growwe ongeregverdigde gevolgtrekkings omtrent die egtheid van die toetse vir mensbloed word steeds gemaak. Moderne serologiese tegnieke maak dit moontlik om die doelmatigheid van dogmas te herbepaal wat op 'n gebrekkige begrip van die perke van die roetine-laboratorium gebaseer is.

Weens hierdie redes is die kwantitatiewe werk waaroor elders in hierdie uitgawe deur dr. J. E. Duncan Taylor gerapporteer word, van spesiale belang, veral in Suid-Afrika, waar die probleem wat geskep word deur die moontlike verwarring met nie-menslike primaat-bloed baie reëel kan wees.

Dr. Duncan Taylor se navorsing was in Durban uitgevoer as personeellid van die Patologiese Laboratorium van die Unie-Departement van Gesondheid—'n laboratorium wat in die jongste tyd uitstaande bydraes tot mediesgeregtelike navorsing gelewer het.

Die huidige strydvraag is hoofsaaklik prakties van aard, want van die rapport van die geregtelike seroloog mag 'n beslissing afhang wat die lewe van 'n beskuldigde raak; nogtans word dit nie algemeen begryp nie dat daar so 'n nou verband is tussen 'n serologiese reaksie van die mens sowel as ander primate tot anti-menslike serum wat uit konyne voorberei word, dat die reaksie in die toetsbuis nie onderskei kan word nie deur die gebruiklike roetinemetodes wat in die bestaande medies-geregtelike handboeke uiteengesit word.

Dr. Duncan Taylor se werk is 'n deeglike oorsig van huidige metodes en ontbloot hulle tekortkomings weens hul onbepaaldheid. Die omvattendheid van haar navorsing word weerspieël in die aansienlike reeks diere wat getoets is, wat dwarsdeur die hele diereryk van visse tot voëls strek.

Een gevolgtrekking blyk duidelik uit haar ondersoek, nl. dat daar geen eenvoudige, praktiese metode vir 'n laboratorium-toets beskikbaar is nie wat menslike bloedvlekke van bloedvlekke van ape (met inbegrip van bobbejane) of lemurs, bv. die nagapie, onderskei. Dis klaarblyklik dat die medies-geregtelike implikasies van hierdie toedrag van sake baie belangrik is. Haar uitstekende ondersoek het dit duidelik laat blyk dat die grootste versigtigheid met die opstel van rapporte wat vir ons Howe bedoel is, beoefen moet word, sodat die indruk nie geskep word nie dat die toetse definitief bewys dat 'n vlek die van mensbloed is

(basing himself on the current routine laboratory methods of investigation) dogmatically asserted that a blood stain was in fact of human origin, could undoubtedly be cross-examined very severely and devastatingly and find himself unable to maintain the dogmatic assertion that the blood stain was exclusively of human origin. It is unlikely that he can go beyond classifying the stain as belonging to the primate group, i.e. the higher anthropoid apes such as the gorilla, the gibbon, the chimpanzee, the orang-outang; and monkeys, baboons and lemurs.

From Dr. Duncan Taylor's work it is clearly inaccurate and misleading even to report that a blood stain is of human or anthropoid origin. The term 'anthropoid' means resembling *anthropos* or Man; its use is, therefore, restricted to those tailless apes which resemble Man. Dr. Taylor's work exposes this vulgar error. Such inexactitude in terminology should be avoided rigorously as it reveals a lack of acquaintance either with the serological problems involved, or with zoological nomenclature.

Although it is clear from Dr. Duncan Taylor's survey that no simple practicable method is available for routine testing, the important fact emerges that where the gravity of the case warranted the trouble, the specific identity of a particular stain probably could be established. The technique required, however, is elaborate, expensive and time-consuming, and would mean that the appropriate primates would have to be inoculated in order to obtain the specific anti-sera for performing the tests.

Apart from the medico-legal importance of this kind of work, it obviously has considerable significance for anthropological and evolutionary studies. It emphasizes, moreover, the great care, knowledge, skill and caution needed to carry out this kind of investigation and to give expert evidence about it.

nie. 'n Deskundige getuie wat (deur homself te verlaat op die gebruiklike metodes van roetine laboratorium-ondersoek) dogmaties verklaar dat 'n bloedvlek in werklikheid van menslike oorsprong is, kan seer sekerlik baie drasties en verwoestend gekruisvra word, en bevind dat hy nie in staat is nie om die dogmatiese verklaring, dat die bloedvlek uitsluitlik van menslike oorsprong is, te handhaaf. Dit is onwaarskynlik dat hy verder sal kan gaan as om die vlek te bestempel as behorende tot die primaat-groep, d.w.s. die hoër mensape soos die gorilla, die gibbon, die sjimpansee, die orang-oetang; en ape, bobbejane en lemurs.

Volgens dr. Duncan Taylor se werk is dit duidelik foutief en misleidend om selfs te rapporteer dat 'n bloedvlek van menslike of antropoïëde oorsprong is. Die uitdrukking ‚antropoïëde' beteken lykende na *anthropos* of die mens, en die gebruik daarvan is derhalwe beperk tot daardie stertlose ape wat na die mens lyk. Dr. Taylor se werk stel hierdie growwe fout aan die kaak. Sulke onnoukeurigheid van terminologie moet streng vermy word, want dit verraai gebrek aan kennis van òf die betrokke serologiese probleme òf die soölogiese benaming.

Hoewel dit duidelik uit dr. Duncan Taylor se oorsig blyk dat daar geen eenvoudige uitvoerbare metode vir roetine-toetsing is nie, tree die belangrike feit te voorskyn dat in 'n geval waar die erns van die saak die moeite regverdig, die spesifieke identiteit van 'n sekere vlek moontlik bepaal kan word. Die vereiste tegniek is egter uitvoerig, duur en tydrowend, en sal beteken dat die gepaste primate ingeënt sal moet word, ten einde die besondere anti-serums om die toetse mee uit te voer, te verkry.

Benewens die medies-geregtelike belangrikheid van hierdie soort werk, het dit klaarblyklik aansienlike betekenis in verband met antropologiese en evolusionêre studies. Bowendien benadruk dit die groot sorg, kennis, bedrewenheid en versigtigheid wat nodig is om hierdie soort van ondersoek uit te voer en deskundige getuienis daaroor af te lê.

# THE GENERAL PRACTITIONER AND THE GENERAL ADAPTATION SYNDROME*

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> 'Sweet are the uses of adversity
> Which, like the toad, ugly and venomous,
> Wears yet a precious jewel in his head.'[1]

Selye's theories of adaptation[2] will certainly have one effect on the general practitioners: Cortisone and ACTH will be prescribed freely. It would be a pity if these exciting new theories made no further impact on general practice. From his unique vantage point over so much of his patients' life span, the general practitioner is ideally placed to assess any academic theories of adaptation. Within the observation of every practitioner, thousands of individuals fight out the collection of struggles which constitute their lives. Fate sometimes presents such a struggle under the conditions of a clean-cut experiment; these occasional cases constitute an ideal test for the truth of any theory.

I propose to present a few such examples sorted from my own experience. This sort of clinical experience, on the whole, is easily explained in terms of Selye's theories and indeed these brilliant theories have illuminated retrospectively much that was dark and puzzling in the clinical scene. However, the clinical evidence is at times absolutely at variance with some of the laboratory theories. Where these clash I have preferred to believe the clinical evidence.

These theories have a further value to the practitioner: he may actually base his treatment on them. The results of such 'Heuristic' experiments will occasionally have outstanding value as confirmation of the theory itself and

*The References will be published at the end of the concluding part of this article.

the practitioner may sometimes be rewarded with a gratifying cure. Admittedly unconfirmed theories are not ideal therapeutic weapons but they are superior to mere placebo treatment.

The General Adaptation Syndrome (G.A.S.) has met with a cool reception from a minority (notably Pickering[3]), but within the limited scope of this article I shall attempt no criticism of the main facts and theories relating to adaptation. I present them herewith and propose to accept them tentatively, so that their clinical implications may be tested:

1. *Adaptation to mild stimuli* is continually occurring. The body is adapting itself to the products of its own metabolism (internal adaptation). The body also adapts itself to the thousand petty shocks of every-day existence (external adaptation). Claude Bernard[4] was the first to point out that all such adaptation has as its 'aim' the constancy of the internal environment or *milieu interieure*. The body struggles to maintain not merely its biochemical norms; in the face of adverse factors, extraordinary efforts are made to preserve the norms of histological pattern, of gross anatomical structure and of such biomechanical values as arterial blood pressure. It is important to realize these vast implications of Claude Bernard's concept, for Selye has shown that exhaustion of the power of adaptation in any one field will affect the power to adapt in a totally different field.[5, 6]

2. Selye's work is concerned with *adaptation to gross stimuli*. He calls such stimuli stressors. (Stress is the *state* produced by a stressor.) The great merit of his work is that he showed that there is the same reaction to every sort of unfamiliar stressor. This is non-specific adaptation. However, when the body has learned to cope with a particular stressor it does so by means of a *specific adaptation*. Non-specific adaptation is quite dependent on the adrenal cortex. Thus a healthy man may be well adapted to some specific stressor such as intense cold. If he now loses his adrenal cortex he can still cope with the cold and he does so in virtue of a specific adaptation which he had previously acquired. But if such an adrenalectomized man is suddenly presented with a completely new stressor, such as an excess of heat, he will die. Alternatively, he would have lived if he had retained the use of his adrenal cortex, which would have furnished him with the material for non-specific adaptation. This latter adaptation tides over the dangerous gap before the body has learned specific adaptation to a particular stressor.

3. Two different hormones are successively secreted by the Adrenal Cortex to effect *non-specific adaptation*: First, gluco-corticoids of which Cortisone is the chief available type; gluco-corticoids are so called because (among many other actions) they have the property of transforming proteins into glucose. The second hormone is of the mineralo-corticoid group and its chief available type is desoxycorticosterone acetate (DOCA). One of the properties of mineralo-corticoids is to control the retention of minerals such as sodium. Both these types of hormone are secreted from the adrenal through the agency of anterior pituitary hormones. The adreno-corticotrophic hormone of the pituitary (ACTH) is responsible for the release of Cortisone but the anterior pituitary hormone which causes the release of DOCA has not yet been identified with certainty. An unknown factor causes the first stage of the General Adaptation Syndrome (G.A.S.); Cortisone causes the second stage and DOCA the third stage. (Often for the sake of brevity in this paper, Cortisone must be taken to imply several gluco-corticoids including, and with a similar action to, Cortisone; DOCA implies several mineralo-corticoids, including and with a similar action to DOCA). Each of these three causative factors is mutually inhibitory to the other. It is as though the actors in each successive scene of a play had not only to act their own role, but also to eject from the scene those actors who came before them, as well as those destined to succeed them in the later scene. The importance of these mutual antagonisms will appear later.

4. There are three stages in the G.A.S.:

(a) *The Stage of Onset, Shock or 'Alarm Reaction'*. Its features are low blood pressure, low temperature, leucopenia, low blood protein, low blood chloride, liability to gastro-duodenal ulceration and extravasation of plasma from the capillaries with resulting haemoconcentration. Selye has called this the stage of damage.[6] However, it is unthinkable that such a clearly defined pattern could represent anything but a definite and organized plan for the body's welfare. This stage is probably the stage of mobilization of the body's defences; as such, we can understand that it may disrupt the smooth working of the body's normal mechanisms. Sometimes this large-scale interruption may prove fatal. In this respect events will have followed a well-established course and I drew attention to this law in a previous paper[7]:—'All defensive mechanisms can become exaggerated until their offensive exceeds their defensive value.' This law will be found to apply to both the DOCA and to the Cortisone phase of the G.A.S.

(b) The next stage is that of *Resistance*. It is mediated by gluco-corticoids and is characterized by a rise in all those values, which fell in the Alarm Reaction and by a healing of alimentary tract ulcers. There is an abrupt fall of eosinophils. Next comes the stage of healing fibrosis; it is mediated by mineralo-corticoids which cause the growth of fibrous tissue around wounds and inflamed areas (locally conditioned target areas of Selye). Selye claims to have produced rheumatoid arthritis experimentally by this mechanism[8]; he injected an irritant around the joint. The general effect of the irritant was to induce a G.A.S. with production of mineralo-corticoid; the latter produced its fibroblastic effect locally upon the joint, because this had been 'conditioned' by the irritant around it; simultaneous injection of Cortisone prevented the development of this experimental rheumatoid arthritis. 'Conditioning' of the pituitary by a high protein diet led to increased production of mineralo-corticotrophic factor during the course of the Alarm Reaction. 'Conditioning' of the kidney by excess of dietary salt causes the kidney to respond to DOCA by the production of yet another hormone Renal Pressor Substance. This RPS raises the blood pressure by causing arteriolar spasm. It can also cause gross arterial lesions and experimentally Selye has used it to produce lesions resembling intimal atheroma, Buerger's disease and periarteritis nodosa.[9] The site and type of the lesion in each case is presumed to depend upon locally conditioning factors. Again we see an example of the previously quoted law, that a beneficial factor may be exaggerated to become an offensive factor.[7] While DOCA is the chief offender in this respect, no stage of the G.A.S. is exempt from the risk of this grim law. Even the highly prized Cortisone can, in excess, cause diabetes, failure of healing, infection, Cushing's syndrome and acne.

(c) With continuous application of the stressor, the last stage eventually appears. This is the stage of exhaustion. There is now complete loss of all types of adaptation. This stage resembles the initial stage of Alarm (Mobilization). There is a fall in all normal levels and this heralds the onset of death.

As stated immediately above, when there is a continuous large-scale demand for adaptation, the power to adapt is eventually exhausted and the patient dies. This led Selye to postulate that every individual is born with a fixed amount

of 'Adaptation Energy'[6] and that when this supply is exhausted the individual has totally lost his power to adapt.

We need not accept this view, because there are at least two ways of becoming bankrupt. It is true that a man with a fixed capital will become bankrupt when he has spent it all. It is also possible for a man with an income to become bankrupt, if his expenditure exceeds his income and it continues to do so until his capital is also exhausted.

I propose the conception of a constant production or income of Adaptation Energy which may be stored (up to a limit), as a capital reserve of adaptation. Later I shall show that this conception best explains the clinical and Selye's own laboratory findings. It is possible that, had Selye's experimental animals been asked to spend adaptation at a lesser rate (below their energy income), they might have coped successfully with their stressor indefinitely.

However, Selye believes that every individual is born with a fixed quantity of 'Adaptation Energy'. According to this theory he can use up this capital entirely in adapting to one stimulus only, whether specific or non-specific; or he can spend it by using smaller amounts of adaptation on each of a great number of different stimuli; but when he has spent all his adaptation in one way or another, he dies.

Before proceeding further, the immense implications of Selye's theory must be realized. He is suggesting that all human experience and hardship weakens an individual in his power to cope with different stressors and that ultimately he can no longer cope with the original stressor. Other scientists have held the view that previous hardship causes a rise in the individual's general power of adaptation. Even common human experience seems to speak with two voices on this matter: since the time of Sparta it has been believed that a man may be toughened by previous hardship, so that eventually he can resist almost any strain. It is also believed that a man may be weakened by previous hardships, so that he falls an easy victim to subsequent strain.

## FURTHER EVIDENCE SUGGESTING THAT PREVIOUS STRAIN WEAKENS AN INDIVIDUAL

Selye subjected batches of rats[6] over a period of about 10 days to various sorts of severe alarm stressors such as cold, extreme exercise and different poisons. Each batch received only one sort of stressor at first. When such a batch was subjected to a second and different stressor they took it very badly and had a much higher death rate than when subjected to their first stressor. No such mortality occurred if the second stimulus was the same as the first, i.e. they had learned and now possessed, a store of specific adaptation energy. This suggests that death was due to a bankruptcy in non-specific adaptation energy. This view is confirmed by the fact that death occurred very quickly, i.e. in the stage when non-specific adaptation normally comes into play.

These results are surprising. We believe that adaptation to drugs such as morphine and alcohol can occur, but it is adaptation at a price; the individual can tolerate more of his drug, but with this tolerance his general health is enfeebled. Clinically we have learned to expect that such a drug taker adapts badly to the strain of operation or disease. However, it is a surprise to learn that the 'physiological' stressors (such as cold and exercise) also result in a lowered tolerance towards any different second stressor. Previous adaptation to exercise resulted in a lowered tolerance towards cold and *vice versa*.

We may not accept Selye's grim view that a creature is born with only a fixed quantity of adaptation energy. However, very great credit is due to him for his experimental work. He has been the first to prove an incredibly simplifying law: Adaptation Energy is like money; it may be spent in one large project or it may be used up in a multitude of *different* petty expenditures.

Apart from laboratory work there is also a good deal of clinical evidence to support the view that previous adaptation to one stressor may cause decreased resistance to a subsequent different stressor:

(a) Pneumonia frequently 'supervenes' after a fracture, particularly a fracture of the femoral neck in old people. I have seen fatal pneumonia rapidly follow upon simple, bilateral tibio-fibular fractures in an old man. Selye has produced such pneumonias experimentally and considers that their development is favoured by the oedema of the lung (local conditioning factor) which follows on the universal increase of capillary permeability characteristic of the Alarm Reaction.

Pneumonia may also follow great exposure to the stressor of severe cold. Here, in Selye's theory, we find at last an explanation of the age-old conception that a 'chill' is dangerous. Intense cold, acting as a stressor to initiate the G.A.S. experimentally, can routinely cause gastro-intestinal ulceration as a part of the Alarm stage. In conjunction with Corbett, I reported a clinical case where death occurred from gastro-intestinal erosion after intense cold[10]; at the time (1940) we were unaware of Selye's theory.

(b) In malarial areas trauma will often 'light up' an otherwise latent malaria. An apparently healthy young soldier was admitted to an equatorial military hospital (itself situated in a non-malarious spot). I operated on him for hernia. Post-operatively he developed high fever and blood examination showed malignant tertian parasites; it seemed very probable that the malarial parasites had been present before operation, although he had never had any clinical symptoms of malaria; he had been able to adapt himself completely to the presence of the parasites until the preliminary stressor of the operation had exhausted this adaptation to malaria.

(c) A patient had been in hospital several weeks (presumably far beyond the incubation period of typhoid fever) when I finally operated on him. Post-operatively his temperature rose steadily in step-ladder fashion. As no other cause could be found for his pyrexia, a Widal test was eventually done. This was of diagnostic titre and there seemed little doubt that he was now suffering from typhoid fever. There were no other cases in hospital or indeed in the district. The strictest enquiry could reveal no possible source of infection, not even from gifts of food. The conclusion seemed inescapable that he was a latent typhoid carrier and that resistance to his own bacilli had been lowered by the stressor effect of the operation.

(d) A remarkable association between severe exercise and liability to poliomyelitis has been demonstrated, both clinically and experimentally.[11] It cannot be doubted that those who are exposed to the infection are more likely to take it and to take it severely, if they have just undergone severe exercise. There has been much recent evidence to suggest that injection of pertussis vaccine may induce liability to poliomyelitis. The relation to Selye's theory is obvious: The first vaccination has acted as a stressor so that there is diminished adaptation energy available for coping with the infection of poliomyelitis.

(e) Examples such as these could be multiplied. In all such cases expenditure of one type of 'Adaptation Energy' has resulted in a scarcity of a different type of 'Adaptation Energy'. Presumably many different specific systems of adaptation and also Non-Specific or General Adaptation all share some essential common component. Thus expenditure of Non-Specific Adaptation may result in scarcity of previously acquired specific adaptation.

A striking difference should be noted between the above clinical observations and Selye's experimental observations on rats. In the clinical cases disease followed quickly on the heels of the initial physical stressor; in the experimental cases there was an interval of about 10 days between the initial stressor and the final fatal stressor. This period is roughly 1/60 of a rat's life cycle. In terms of a man's life this is about one year. There is absolutely no shred of clinical evidence to suggest that about a year or more

# Centanaest Combined Anaesthetic Apparatus

The Centanaest Combined Anaesthetic Apparatus is designed for the administration of any of the following anaesthetics: Nitrous Oxide, Cyclopropane, Ether, Chloroform, Trilene and Oxygen by open, semi-open or closed circuit technique.

The Cabinet is attractively finished in green enamel, with all bright parts chrome-plated. Two drawers are provided for the storage of Accessories. The whole unit being mounted on four-inch castors.

A feature of the Machine is the fact that prior to using the Carbon Dioxide Absorber, it is necessary to disconnect the Ether and Trilene Vapourisers thus preventing the accidental use of Trilene in a closed circuit with Carbon Dioxide absorption by Soda Lime.

A Coxeter-Mushin Mark II Carbon Dioxide Absorber is incorporated.

The Apparatus accommodates:

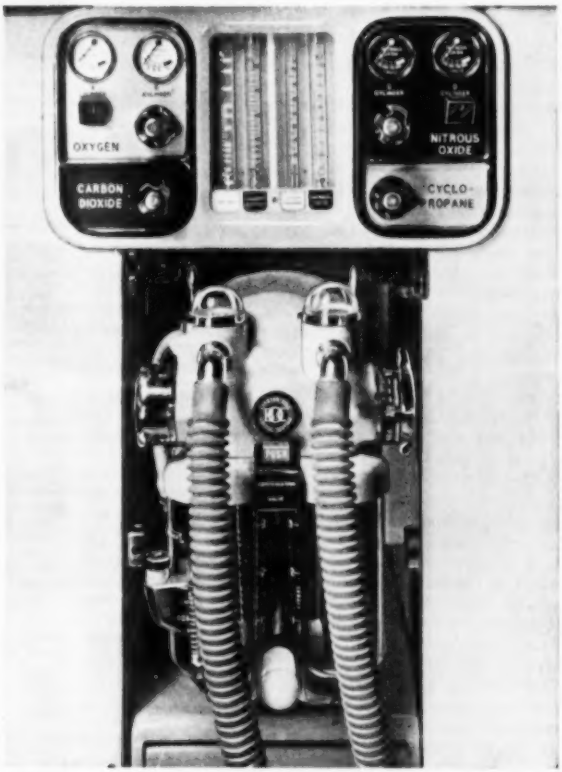
2 x 10 cubic feet Oxygen Cylinders;

2 x 200 gallons Nitrous Oxide Cylinders;

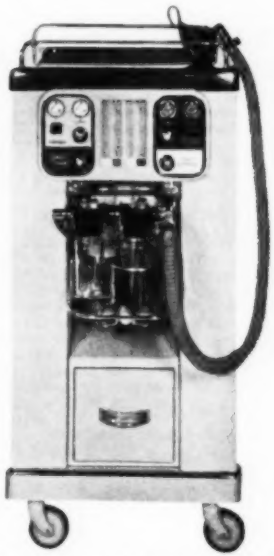
1 x 2-lb. or 4-lb. Carbon Dioxide Cylinders;

and 1 x 25, 50 or 100 gallons Cyclopropane Cylinder.

These are accommodated in recesses on either side of the Machine and are connected by means of screw clamp yokes.




The control panel which incorporates a Coxeter Quadruple Rotameter Unit for accurate flow-rate measurement of the Gases. Flow control knobs for Oxygen, Carbon Dioxide, Nitrous Oxide and Cyclopropane are conveniently situated, and By-pass Buttons are provided for "flooding" Oxygen and Nitrous Oxide. Independent control gauges are provided for each Oxygen and Nitrous Oxide Cylinder.



The Machine assembled for the administration of Nitrous Oxide, Ether, Chloroform or Trilene/Oxygen combination by semi-closed method, the standard Magill Re-breathing Unit being used.

after a severe alarm reaction, a man has less power of adaptation to other stressors (such as accident, operation or disease). If anything the contrary appears to be true.

EVIDENCE SUGGESTING THAT PREVIOUS ADAPTATION STRENGTHENS THE INDIVIDUAL TO RESIST FUTURE STRESSORS

(a) Alexis Carrel[12] has been the foremost proponent of this view. He points out that when an individual fails to react to certain stimuli, he may react to them after he has been forced to react to a totally new stimulus. Thus men moved to mountain air, where they must forcibly adapt to a lower oxygen tension, immediately become more vivacious and reactive to stimuli generally. The abrupt stimulus of a cold shower produces a similar effect. In other words, the necessity for adaptation to one stimulus has awakened and increased the power of reacting to many other stimuli. (This view is a logical converse of Pavlov's theory which regards sleep as a spread of inhibition over the whole cortex, as a result of the functioning of a single inhibitory reflex.)

Carrel's views are a matter of everyday observation but, before him, no one had expressed the matter in clear language. It is surprising that such a master of the experimental method as Carrel should have been content to leave this valuable theory without experimental support; it should be tested under controlled laboratory conditions. It would be especially interesting to be able to prove that the increase in adaptability ranged throughout the nervous biochemical and immunological systems, so that the necessity for adaptation in any one of these systems awakens all the others. It should be noted that Carrel's theory relates only to minor stimuli; unlike Selye's, his were less severe than Alarm stimuli.

(b) For centuries physicians have been aware that a change of air or resort to a bathing establishment had curative value in chronic disease. It is possible that the physician, in ordering a change of air, may have wished to rid himself of the embarrassment of a patient whose disease he could not cure. But whatever the motive, there is no doubt that such treatment is often effective. Nor can such success be explained away by the assumption that the new environment is less favourable to the *modus vivendi* of the causative bacteria; for no greater contrast can be imagined than between the climates of Switzerland and the Cape Province coast. Yet vast numbers of English consumptives have been cured by either climate.

Incidentally the Cape Province does not seem to be unfavourable to the development of tuberculosis for those actually born in the province. If Carrel's theory is correct we ought to send South African consumptives to England for the cure!

I saw a remarkable instance which proved the beneficial effect of climatic change on the course of tuberculosis. In 1940 I was on a ship which passed through the Panama Canal on its way to England. At the Canal Hospital I was called into consultation over the case of a British steward. Several months before he had been left behind by his ship because he was suffering from such severe pulmonary tuberculosis that he was too ill to proceed. Since then his condition steadily deteriorated until now he was a mere skeleton with a swinging temperature, a large cavity in his left apex and sputum crowded with tubercle bacilli. He was determined to travel back with us to England. In vain I pointed out the disadvantages and dangers of travel under war-time conditions to a man in his state of health.

Finally, I was forced to say that the change to the cold English winter might prove a grave danger to his life. 'Doctor,' he said, 'if I am to die, I would like to finish among my own people!' After that it was impossible to refuse him. He came with us on our long journey and the ship went steadily northward, making a wide detour to avoid enemy submarines. The climate grew rapidly more icy, but even when we approached the Arctic circle he appeared to be holding his own well, in fact I was forced to admit to myself that he seemed to be improving rapidly. Somewhere between Iceland and the Hebrides the ship was torpedoed and the survivors drifted in open boats over a near-Arctic mid-winter sea. A few days later in a Northern Scottish hospital I was surprised to see this man alive. Not only was he alive but his ruddy complexion, firm flesh and brisk movements signified a fine degree of health. He was now symptom-free and, in the radiograph, evidence of his former large cavity was detectable only with difficulty. The sputum was negative. It was hard to believe that this was the half-dying man I had first seen only a month ago; the conclusion seemed inescapable that his remarkable transformation had been due to the change to an 'adverse' climate.

In Selye's experiments on rats a previous history of fairly remote exposure to a severe Alarm stimulus appeared to render them less fit to face future different stressors. Is this true of human beings? We must be careful to differentiate this problem from those in the preceeding paragraph where the reaction to mild stimuli was discussed. Practitioners have had much experience of soldiers exposed to great extremes of temperature, exhausting physical fatigue and periods of prolonged starvation; we know the reactions of Natives, whose lives have been a succession of such incidents; we have observed numbers of men addicted to strenuous and exhausting sports. It has already been conceded that all such men, as an immediate result of their severe preliminary stressor, are more liable to death from disease and trauma. But when this transient phase of susceptibility has passed, what is their reaction to severe trauma, both accidental and surgical and how do they react to sudden grave infection? Have such men been toughened by all their past trials or have they (according to Selye's views) been weakened by previous expenditure of a fixed capital of Adaptation energy?

Often the modern city has sprung up rapidly from the bare veld and at the periphery of the great blocks of luxury flats there still linger men of all colours who have survived the hazards of life under conditions of bitter stress. Thus there remains a fleeting opportunity for the city practitioner to compare the two classes of humanity. Admittedly there are factors which blur the issue. Alcoholism and syphilis are much commoner among those who have led the hard life and this would enfeeble their reaction to stressors. On the other hand, such men have a cheerful contempt for stress, as high morale often goes with low morals; and morale has a powerful though ill-defined effect upon survival under stress. When all these factors have been assessed and discounted I can give my own view without hesitation, based upon 25 years of practice: those who have led the hard life withstand trauma and acute disease as well as, if not better than those whose lives have been soft. I can even call to mind some remarkable cases of resistance on the part of patients who had lived the hard life. South African Natives have the reputation of being practically 'shock proof' after severe trauma. From all this clinical experience it is clear to me that men can re-create their spent capital of Adaptation Energy if given time to do so; there is an 'Energy Income' which may be saved to provide fresh capital. It is probable that the rate of income decreases with advancing age. Thus this part of Selye's theory receives no support from clinical observations. However, Selye's facts are explicable on an amended theory which I shall propose later in this paper.

It is strange that from the French-Canadian laboratory of Selye should have emanated this theory that previous adaptation weakens an individual. More than a century

ago from the same part of the world, came an account of resistance unsurpassable in the human story:

Alexis St. Martin, the French-Canadian voyageur, his body hardened and toughened by a life of continuous struggle accidentally discharged his own shotgun into his chest and abdomen. Beaumont,[13] the American surgeon, has written the classical account of this man's prolonged sufferings and amazing resistance. The patient was eventually left with a permanent gastric fistula through which Beaumont studied his gastric mucosa. Both before and after his terrible injuries, St. Martin's life was one long round of exposure and hardship in bitter climatic conditions. Beaumont relates how he paddled his canoe, fully laden with his wife and children and all possessions, for thousands of miles even before his wounds were properly healed.

Lately, Sir Adolphe Abrahams[14] has given an interesting account of the autopsy on a man who died of malignant disease of the thyroid:

In his youth this man's feats as a long-distance cyclist had been legendary; he was probably the greatest long-distance cyclist of all time. At the age of 18 he had broken the record for the Land's End to John O'Groats trip (over 600 miles). He repeated this great feat of endurance no less than 24 times, although contemporary physicians warned him that each feat would cost him 10 years of his life. In spite of thus losing 240 years of his life he lived to the age of 78 years and autopsy disclosed a remarkably healthy heart and coronary vessels. All other viscera appeared healthy.

*(To be concluded)*

# SPINAL ATROPHIC PARALYSIS

## FOLLOWING LIGHTNING STROKE

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In South Africa where violent thunderstorms are frequent in summer, death due to lightning stroke is common. It is surprising that amongst those who survive, complete recovery is the rule and neurological complications are very rare. Amongst survivors the immediate results are shock, suspended animation and frequently kerauno-paralysis, i.e. a transient flaccid paraplegia with objective sensory loss, which may be accompanied by disorders of the extrapyramidal system and by changes in the electro-encephalogram (Patterson and Turner, 1944). Superficial burns, especially along the skin creases and beneath metallic objects in the clothing, invariably occur.

Several neurological disorders have been described following lightning stroke, but Panse (1930) (cited by Critchley, 1934) considers spinal atrophic paralysis, a condition closely resembling amyotrophic lateral sclerosis, to be the characteristic sequel.

### CASE REPORT

Three months before admission to the hospital, a Mauritian carpenter aged 46 years was struck by lightning near some trees on his way home across the veld. He was quite certain no rain had fallen before he was struck. He was found unconscious in a ditch two hours later and was taken to the local hospital where he regained consciousness the next afternoon. He was found to be suffering from shock and extensive second degree burns of the trunk and lips. The front of his hat had been burned off and the rest of his clothing severely damaged.

His burns were slow in healing and it was six weeks before he was fit to be discharged. During that period no neurological abnormalities had been found.

Two weeks before admission here he developed a transient pain between the shoulder blades and an aching of the muscles of the hands. A week later he felt pins and needles in his finger tips spreading up to his elbows. Shortly afterwards he had spasms of the flexors of the fingers and later was unable to clench his fists. He then sought medical advice and was admitted to this hospital on 14 May 1950.

Examination showed him to be a thin, intelligent man. The scars of his burns were very prominent. The lower lip was burned, the neck escaped and the burns started again at the upper end of the sternum and ran down to the abdomen, branching out to both groins. The thighs were not involved but there was a small burn just above the left ankle.

No further abnormalities could be found except in the central nervous system where the signs were much more pronounced on the left side of the body.

*Head and Neck.* While the tongue was not wasted there was a marked fibrillary tremor of it and the muscle of the lower lip.

*Upper Limbs.* Power and tone were diminished in both arms and he was unable to flex the fingers of his left hand fully. There was definite muscular wasting and fibrillation in the small muscles of both hands. Fibrillation was also seen in all the muscles of the left arm and in the left pectoralis major. This was intensified by the injection of Prostigmine.

All the reflexes were exaggerated and both Wartenberg's sign and Hoffman's reflex were easily elicited.

*Lower Limbs.* Power was reduced in both legs and he could walk only with difficulty. Tone was increased but there was no apparent muscular wasting or fibrillation.

The knee jerks were exaggerated, but neither the ankle jerks nor the planter reflexes could be obtained. Perception of pin prick was diminished over both feet as high as the ankles. No other abnormality of sensation was found.

### INVESTIGATIONS

*Blood*: Haemoglobin: 12.95 gm. %.
White blood cells: 4,800 per c.mm.
*Cerebrospinal Fluid*:—Protein: 50 mg. per 100 c.c.
Globulin: Moderate excess.
Cells: 6 lymphocytes per c.mm.
Chlorides: 730 mg. per 100 c.c.
Lange curve: 1344443311.
*Wassermann Reaction*: Negative in blood and cerebrospinal fluid.
*Urinary Lead Excretion*: 0.020 mg. for 24 hours.
*Chest X-ray*: Normal.

*Treatment and Progress.* It was decided to try the effects of vitamin E on this patient and 500 mg. of alpha-

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tocopherol were given daily in divided doses for five weeks. Massage and movements were started at the same time and three weeks later, when there was definite improvement, faradism was commenced.

Progress was slow but steady and after three weeks he was able to close his fists. On discharge six weeks later, power in the arms and legs was appreciably increased and he could walk well. The muscles remained unchanged in bulk, but fibrillation was diminished and could be found only in the tongue and the small muscles of the left hand. The tendon jerks were unaltered but the plantar reflexes had reappeared and were flexor in character. All sensory abnormalities had disappeared.

### DIAGNOSIS

Superficially this case resembled amyotrophic lateral sclerosis but there were two main points of difference. The disease had only started after he had been struck by lightning and, after rapid initial progress, a steady improvement had set in. This is unlike amyotrophic lateral sclerosis which, if rapidly progressive, seldom remits (Brain, 1947).

The second main point of difference was the finding of an abnormal spinal fluid. In amyotrophic lateral sclerosis the fluid is invariably unchanged (Walshe, 1947).

Syphilis and lead poisoning, both rare causes of motor neurone disease, were considered. No evidence of these conditions could be found, however, either in the history or the clinical and laboratory examinations.

### DISCUSSION

In fatal cases of lightning stroke the pathological findings are highly characteristic and consist of a violent disruption of the tissues and blood vessels of the brain. Abnormal rents and fissures occur with splitting apart of the cortical layers. The cerebrospinal and perivascular spaces are distended and the ganglion cells are damaged. The blood vessels, especially those at the base of the brain, are injured and the muscular coats of even large vessels may be torn (Pritchard, 1934). In addition Critchley (1934) describes scattered petechiae throughout the brain, medulla and spinal cord, especially around the anterior horn cells. Changes also occur in the peripheral nerves and muscles.

The manner in which high voltage currents cause damage to the nervous system has been discussed by Blake Pritchard (1934). He has shown that neither electrolysis of the cerebrospinal fluid nor the heating effects of the charge as it passes through the body can produce these peculiar disruptive lesions. Instead he has shown mathematically how they may be produced by electrostatic forces and his arguments may be summarized thus:—

If a man is struck by lightning when wet through and thus making good contact with the ground, the charge will rapidly flow over him to earth. Burns will be the main result. If, however, the man is dry and thus fairly well insulated from the ground the charge, not being able to escape rapidly, will accumulate on the surface of his body. The mutual repulsion of the similarly charged surface particles will exert a sudden powerful force outwards and the entire body surface will tend to expand away from the body. This force will be communicated inwards as a sudden wave of decompression. As a result, fluid spaces will be distorted and tissues such as the brain, having little cohesion, will be disrupted. This mechanism explains the violent stripping of clothes off people struck by lightning.

There seems no reason to doubt the man's statement that he was quite dry when struck, as in a thunderstorm the most severe lightning usually just precedes the fall of rain. He thus seems extremely fortunate to have escaped with his life. Taking into consideration his position when the accident occurred, it is likely that the main flash of lightning struck the trees nearby and that he received only a small portion of the charge. He would otherwise almost certainly have been killed.

### SUMMARY

A case of spinal atrophic paralysis following lightning stroke has been described and the resemblance to amyotrophic lateral sclerosis noted.

The main pathological findings in death due to high voltage electrical currents, and the possible mechanism causing these injuries, has been discussed.

I wish to express my thanks to the house physician, Dr. P. Perrot, for his help with this case, and to Dr. J. Parker for permission to publish this case.

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## PROCEDURES IN THE CONTROL OF TUBERCULOSIS*

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The latter half of the nineteenth century was an age of discovery in medicine—disease after disease was found to be caused by germs and when Robert Koch in 1882 announced to the world that he had discovered the organism responsible for tuberculosis it was felt that the end of this devastating disease was in sight.

Koch also enunciated his postulates, which formed the keystone of the bacterial causation of disease. In brief these postulates were:—

(a) The specific germ thought to be responsible for a particular disease must be found in every case of the disease.
(b) It must be possible to isolate the germ in pure culture.
(c) It must be possible always to reproduce the disease in a susceptible animal. As far as tubercle bacilli were concerned, they could be found in every case of the disease. It was possible to isolate such organisms in pure culture, and

* A paper read at the *Second National Conference on Tuberculosis*, held in Cape Town, on 10 May 1951.

the disease could always be reproduced by inoculation into guinea pigs—so tubercle bacilli were the accepted cause of tuberculosis.

Koch discovered tuberculin, a product of the growth of tubercle bacilli, and stated that the disease could be cured by injections of this material. This latter statement was not true and was the first disastrous failure of many attempts to eradicate tuberculosis.

In 1907 Von Pirquet found that by scratching tuberculin into the skin it was possible to divide all human beings and animals into two classes—those who had a reaction to this procedure and those who showed no change. The explanation of the reaction was that the entry of tubercle bacilli into the body of any animal resulted in the tissues of such an animal becoming sensitive to tuberculin—expressed by local inflammation when tuberculin was scratched into the skin.

A great distinction was now made between tuberculous disease and tuberculous infection. Positive reactors to tuberculin could be divided into infected and diseased by means of clinical, bacteriological and later radiological investigation. The fact was that man did not always behave like a susceptible animal, because infection with tubercle bacilli was not always followed by tuberculous disease. And thus we arrive at the fundamental question in tuberculosis. Why out of a large number of persons who react to tuberculin do only comparatively few exhibit manifest tuberculous disease—and of the diseased why is the process not of the uniform type seen in the infected guinea pig (the standard susceptible animal)?

Let us digress for a moment and consider how the human being reacts to infection in the ordinary way. A tubercle bacillus is inhaled (or eaten), is picked up by a wandering cell and carried to the nearest lymph node. The bacillus multiplies in the cell and eventually kills it. Other cells gather round, pick up bacilli—moving always towards the nearest large lymph glands. These glands eventually become diseased. The process may stop at this stage (Rankes' primary complex) leaving only a positive tuberculin reaction as a sign that infection and disease has taken place or it may spread locally (progressive primary disease).

Some organisms at the primary stage may escape through the thoracic duct or abdominal lymphatics into the blood stream and stick in small vessels in the bones, joints, kidneys, meninges and lungs (Rankes' 2nd stage). Some of the organisms which remain in the lungs, especially the upper parts, multiply and kill healthy tissue and eventually the dead tissue is softened and discharged into a bronchial tube, leaving a cavity which discharges tubercle bacilli intermittently, these bacilli trickling down into other parts of the bronchial tree, starting there new foci of disease (Rankes' 3rd stage). Accidents may happen in this progression, e.g. a diseased focus might open into a blood vessel. The whole body is then flooded with tubercle bacilli and miliary tuberculosis, including meningitis, results.

From the point of view of the clinician we see tuberculosis usually in the 3rd stage in adults, where there is a never-ending struggle between the individual and the bacillus, the lungs usually being the battlefield and the bronchial tree the lines of communication of the organisms. The end result is always the destruction of pulmonary tissue and it is at this stage that the surgeon is so useful to-day as he is able to remove such dead and useless tissue. We see the disease in the first stage usually in children, who come to us with progressive primary tuberculosis. Some of our cases are fulminating—the old 'galloping consumption' moving fast to meet death; others heal rapidly in spite of our efforts. Others occupy a mid-position.

Epidemiologists used to talk glibly of racial susceptibility—the black troops from French Equatorial Africa sent to France in the first World War, the Cape Coloured Corps sent to the same country, exhibited a fulminating type of tuberculous disease called by Borrell and later by Cummings, the tuberculosis of the guinea pig, of the child, to express the extreme susceptibility of these troops. The rapidly advancing fulminating disease in urban Bantu in South Africa to-day, the acute disease met with in mining Natives, have all been ascribed to the fact that certain races have never been in contact with tuberculosis and are therefore 'not salted', and when they meet the bacillus for the first time they succumb rapidly. The theory fitted so well that nobody thought very deeply or critically about it. The fallacy of racial susceptibility could easily be discovered by considering the Egyptians and the Chinese, among whom tuberculosis has been rampant for centuries and was well known before European civilization began. No two races could have been more thoroughly 'salted' and yet the death rate from tuberculosis in these countries is very high and the disease very often of a fulminating type.

There is some evidence to show that certain families have a high resistance to tuberculosis whereas others are extremely susceptible. All clinicians have met with certain families whose resistance to this disease is nil. Lurie of the Phipps Institute has succeeded in breeding rabbit families some of whose resistance is high and who exhibit a slowly progressive disease after infection and others who die rapidly from a fulminating type of disease when infected.

In individuals age has some effect on resistance, young infants being more susceptible than older children, e.g. 10% of all deaths from tuberculosis in Europeans in South Africa occur under the age of five years. Sex has some effect as females appear to be more susceptible during child-bearing age.

But apart from these minor factors tuberculosis is fundamentally a disease of *environmental stress*. Death rates and other significant factors tell the tale. Death rates are high in the adolescent entering into competitive life; high in men growing old and doing a job which is too much for their ageing tissues; high in the poorer sections of any community; high in the non-European in South Africa, especially in urban areas. Very important epidemiological evidence has arisen from our studies in South Africa of tuberculosis in the Bantu in urban and in isolated rural communities. The amount of disease is highest in the urban and least in the isolated rural areas; but the type of disease is usually fulminating in the urban case and slowly progressive in the isolated rural case. The amount of infection is approximately the same.

The only real differences between the urban and rural communities are in food and physical effort. The isolated rural Bantu have a monotonous but adequate diet, the urban a varied, but biologically inadequate diet; the rural Bantu do not work hard physically, the urban do. As the

years have gone on the amount of disease in the rural areas is steadily increasing owing to larger numbers of urban people going home to die, and we find that years of famine result in the appearance of fulminating disease in the community. It is interesting to note here that the death rate in slaves and their masters in the U.S.A. during the days of slavery was approximately equal; a slave was a valuable piece of property and was therefore properly fed and cared for. When slavery was abolished the death rate in negroes in the States was 20 times that of the whites and even to-day is five times as high.

Death rates from tuberculosis are high in countries such as Spain, China, India; and low in Denmark, Holland and the Middle West in the U.S.A.

High rates are found in countries devastated by war. The factors here are complex but the first World War gave an important clue to the value of nutrition—Denmark was exporting most of her meat, butter, eggs and cheese to Britain during the early stages of this War and her death rate from tuberculosis rose rapidly. When the German blockade became effective and the Danes could not export their protective foodstuffs and were forced to eat them themselves, there was a precipitous decline in the tuberculosis death rate preceding the fall in the belligerent countries after the War. The second World War showed the highest rise in death rates in those countries such as Holland where the population was bereft of food and it is of interest to note that some observers actually noted a change in the type of disease from slowly progressive to fulminating during the period when food was at its lowest (Belgium). Britain, with a system of food subsidization and rationing in the Second World War, which enabled the poorest to purchase the protective foodstuffs, did not have the expected epidemic of tuberculosis when thousands of cases of tuberculosis were discharged from Sanatoria to the homes to make room for bomb casualties. The vital importance of proper rationing spread over years is seen in the spectacular drop in the death rate from tuberculosis in Great Britain in the first half of 1950 (17% in the first half of 1949) and in the fact that in spite of greatly increased diagnostic facilities which lead to more cases being discovered after the War, the present trend even of new cases is downward (5% decrease in the first six months of 1950 over a similar period in 1949).

A factor of importance in resistance is the presence of other diseases. We all know, e.g. that diabetics are especially prone to develop tuberculosis, but we have also found in South Africa that the greater the number of other diseases found in the Bantu, the more fulminating the tuberculosis and that when the other diseases are eliminated (intestinal parasites mainly) the process of healing of tuberculosis is hastened.

All these facts lead us to some of the major environmental stresses making man a susceptible animal as far as tuberculosis infection is concerned as:

(a) Nutritional.
(b) Physical effort and consequent fatigue.
(c) Crowding leading to infection and repeated re-infection.
(d) The presence of other diseases, mostly dirt diseases due to impure water supplies and poor sewage disposal with a consequent lack of personal and communal hygiene.

Koch's postulates in human beings can only be fulfilled if we turn the human being into a susceptible animal by subjecting him to these stresses. Procedures for the control of tuberculosis that ignore this fundamental fact will never succeed.

If certain environmental stresses in a given community produce X cases of tuberculosis each year, one can remove all these X cases each year and the problem then remains exactly as it was before one commenced one's efforts. Even if we treat cases to cure and return them to a community where stresses are unchanged, they will always break down again—a fact which has been a bitter pill for the clinician to swallow.

There is a modern tendency to control tuberculosis by applying a simple series of procedures, such as mass radiography of the total population—the removal of persons suffering from tuberculosis—curing them, rehabilitating them and returning them to ordinary life. This system of control will not be effective because it ignores the stresses which produce the susceptibles—a case pronounced clear to-day as a result of mass X-ray can be dead of tuberculosis in three months if the environmental stress is sufficiently great.

How then do we proceed to control tuberculosis in any community? A background of epidemiological knowledge, such as I have endeavoured to sketch for you to-day, is essential.

The first step is a thorough investigation of the environment in which the community lives. The following must be known in detail:

(a) Food in all aspects—amount, quality, food habits, including the percentage of milk containing tubercle bacilli.
(b) Housing, especially persons per room.
(c) Work, transport, recreation.
Sewage disposal } Communal hygiene.
(d) Water supplies }
(e) Traditional hygienic habits of the people.

The secure step is to ascertain:

1. *The Number of Persons of All Age Groups Showing Tuberculous Infection.* This is done by tuberculin testing large cross-sections of the community or the whole community if this is possible. If repeated at regular intervals, this procedure will testify to the efficiency or otherwise of the control measures—a declining percentage of positive reactors means good control, a rising percentage of positive reactors means inefficient control.

2. *The Number of Persons Found to be Diseased.* These morbidity figures can be obtained by repeated mass X-ray of large cross-sections of a community, and by conscientious notification of all cases by medical practitioners. The average number of cases found to-day is about 3 in 1,000 in a stable community (Great Britain, parts of U.S.A.), and 7 per 1,000 in unstable communities such as the urban Bantu in South Africa. We have found in some communities, such as large prisons, up to 20 per 1,000—here the disease makes the law-breaker, the individual develops tuberculosis, is too ill to undertake hard physical labour, and becomes a vagrant.

3. *The Death Rate*—accurate figures and the number of persons who die of tuberculosis in a given period (mortality). The only fairly accurate figures of this nature in South Africa are the European and Asiatic rates (? Coloured). The Bantu tend to return to tribal areas to die—and no figures are available for this race.

When these investigations have been completed, we can say with moderate accuracy that such and such environmental stresses acting on our given community will produce in each year X cases of tuberculous diseases from

the number of persons infected with tubercle bacilli, and that on an average N people will die of the disease in the same period.

The next step is to make every attempt to remove or mitigate the environmental stresses, because improved environment will form the real basis of control—the better the environment, the less tuberculosis will emerge. Pasturization of milk, e.g., is one way of eliminating a stress. Concurrently, we ought to isolate the diseased and therefore infectious individuals. The type of isolation to be provided depends on the needs of the patient. Some will need active treatment with antibiotics, chemotherapeutic substances and removal of diseased tissue by surgery.

The last five years have produced a revolution in the treatment of tuberculosis. Particularly, certain non-European cases in South Africa who, in general, a few years ago had a hopeless prognosis, now often have a bright future because the antibiotics and chemotherapeutic substances act best in the type of disease such persons present, and surgeons are thus enabled to remove destroyed lung tissue with safety.

A high percentage of cases will still need isolation only—often best in a rural environment near their own homes—preferably in close association with some medical supervision, such as is provided by Health Centres. Others are best suited to settlement life, either with or without their families, either in peri-urban or in rural areas. Others still can be isolated and even treated in their own homes—this last method of isolation is particularly applicable to Europeans in South Africa. In assesing the number of beds or isolation units needed for the various races in South Africa we must beware of standards suited to other countries. The suggestion in some parts of the U.S.A. that at least 10 beds per death are necessary, the minimum of two to three per death in other countries, is applicable to each country concerned and not simply transferable as optimal for South Africa. Our problem is complex and our requirements in beds, isolation units in settlements and elsewhere will have to be tailored to fit our races, their habits and ways of life and our communal purse. We have found, e.g. that Native children with progressive primary tuberculosis do better in a mission hospital in the rural area when they eat and live according to tradition, than they do in our own hospital in Durban, provided only that medical and nursing care is equal.

Isolation and treatment should be accompanied by occupational therapy and followed by rehabilitation if this is possible. A certain number of cases will be fit only for permanent isolation and sheltered employment.

We have left behind in the community after removing 'the diseased and dangerous' a large number of persons who have a positive reaction to tuberculin. These are the potential cases of tuberculosis and special care should be taken that they do not become active and infectious cases of tuberculous disease. Extra food, the removal of an infectious case from their immediate environment so that they are not subjected to repeated infection which tends to make their lesions unstable, the avoidance of excessive fatigue, the choice of a suitable occupation—these are all instances of such care.

The uninfected (the tuberculin negative persons who are left after we have removed the diseased and cared for the positive tuberculin reactors), are the subject of one of the world's greatest controversies to-day. To vaccinate or not to vaccinate, that is the question agitating the minds of epidemiologists, bacteriologists and clinicians the world over. Vaccination with B.C.G. is being used extensively by most countries in the world except Great Britain, the U.S.A. and South Africa. In Britain, after much deliberation, a cautious use of the vaccine is being made —contacts of active cases, nurses and medical students are being vaccinated and the question of extending vaccination to school-leavers is being debated. In the U.S.A. caution is still advised but large-scale experimental work is in progress. In South Africa we are inclined to the cautious approach of Great Britain and the U.S.A. Our problem, with so many primitive people whose hygienic habits are not helpful in relation to the intradermal use of the vaccine, makes a careful consideration of oral vaccine important.

In all diseases which last a long time and which often do not result in a complete return of earning capacity, the family of a sick breadwinner is subjected to greatly increased economic stress and is consequently very prone to become a susceptible animal in terms of Koch's postulates. Therefore any curative scheme must envisage some method of keeping a family intact by help in money, in kind or by providing a home in a settlement or similar place.

Finally, proper education of the community in hygiene, in the dangers it has to face and the methods of overcoming them, is most important. We need a re-orientation of our form of education of the infectious case. We must not make him feel a leper but should teach him how *not* to infect others and make him a crusader in the non-spreading of tubercle bacilli and thus an active participant in the anti-tuberculosis fight. The intelligent infectious case can be trained to put an invisible barrier of isolation round himself.

The use of chemotherapeutic substances to diminish the amount and infectivity of positive sputum in ambulant cases is one of the important ancillary methods of control.

The talk to-day is not so much of tuberculosis control but of tuberculosis eradication. We are still far from that ideal, but it is not unattainable or impossible; we know what to do and the intelligent practical application of this knowledge will lead to the end of tuberculosis in our country.

## NEW PREPARATIONS AND APPLIANCES

### MICROPELLETS PROFOLIOL—'SCHERING' (CHEMICALLY IDENTICAL WITH PROGYNON BRAND)

*Micropellets Profoliol* may be defined as pure, uniform micro-crystalline oestradiol in aqueous suspension. After injection the saline menstruum is readily absorbed establishing a depot of finely divided, active hormone in the tissues from where it is absorbed at a physiological rate for a period of a week or longer. The high potency of micro-crystalline oestradiol, in *Profoliol Micropellets* far surpass the activity of secondary oestrogens and affords the advantages of rapid effect, uniform absorption and prolonged action.

*Indications*: In all cases of follicular hormone deficiency in which conventional oestrogens are indicated, such as the menopausal syndrome, secondary amenorrhoea, etc.

*Micropellets Profoliol* is administered by intramuscular injection.

*Dosage*: In average menopausal patients 1 mg. weekly, reduced gradually, with good progress, to 0.5 mg. and even 0.25 mg. weekly or every 10 days. A severe menopausal syndrome may warrant 1 mg. twice a week for a short initial period. In other disorders dosage is adjusted to the individual case.

*Packaging*: Available in multiple dose vials of 10 c.c. in a concentration of 1 mg. per c.c.

*Micropellets Profoliol* are manufactured in the Union of South Africa by Scherag (Pty.), Limited, for and under the formula and technical supervision of Schering Corporation, Bloomfield, New Jersey, U.S.A.

*Sole Distributors*: Scherag (Pty.) Ltd., 127 Anderson Street, Johannesburg.

## ASSOCIATION NEWS : VERENIGINGSNUUS

### BARAGWANATH MEDICAL SOCIETY: NOVEMBER (1951) MEETING

### VASCULAR RETINOPATHIES (DR. I. TAYLOR)

*Definition.* The term vascular retinopathy implies an affection or degeneration of the retina caused by disease of its vessels. 'Retinitis' is an unfortunate term for the retinal manifestations of metabolic or cardio-vascular disease, for the essential changes are degenerative in nature, and not inflammatory.

*Some Anatomical and Optical Facts about the Vessels of the Retina.* The central retinal artery is a branch of the ophthalmic artery and histologically resembles other arteries of similar calibre. It has an intima with a single layer of endothelium lying directly on the internal elastic lamina. The media has a well-developed muscle coat.

On entering the eye through the optic disc, the artery becomes markedly altered. The internal elastic lamina becomes reduced to a thin layer and, after one or two branchings, disappears. The muscle coat similarly becomes reduced to a single layer of fibres and after one or two bifurcations no longer forms a continuous layer, but the fibres are separated by small gaps. The whole retinal arterial tree, except for its stem and branches in or near the optic disc, is therefore arteriolar, since arteries without an elastic lamina and continuous muscle coat are by definition arterioles.

*Arterio-Venous Crossings.* The retina is extremely thin—0.56 mm. at the optic disc, 0.18 mm. at the levator and 0.1 mm. at its anterior extremity. At points where the vessels cross they are brought into intimate contact; the endothelium of the vein ties directly on the outer surface of the arterial media with no adventitia intervening. A common adventitia surrounds both vessels.

In vascular disease a variety of changes is observed at the arterio-venous crossings. Any change in the tortuosity of the retinal arteries will drag the vein out of the normal course while longitudinal shrinkage of an artery will drag the crossing towards the shortened segment of the vessel.

The ophthalmoscopic changes characteristic of dislocation of the arterio-venous crossing may be called 'arterio-venous displacement'. If the arterial wall becomes thickened, such as occurs in arteriolar sclerosis, it encroaches on the space available for the lumen of the vein in the common adventitial sheath. This causes partial venous stases and engorgement peripheral to the arterio-venous crossing. This is the 'arterio-venous' nipping phenomenon, first described by Marcus Gunn, and hence known as Gunn's sign.

Vessel wall translucency in the normal eye is so perfect that the vessels are transparent and invisible. A constant early feature of vascular sclerosis is the inability to see the veins through the arterial walls at the arterio-venous crossings, so that the veins appear to be interrupted before and after they cross the arteries, a sign also first noted by Gunn.

*The Light Reflex on the Retinal Vessels.* A normal retinal artery has, ophthalmoscopically, a pale yellowish central portion and two thin dark red lines on either side. The central portion is the light streak, which is the reflection of the ophthalmoscope light at the convex cylindrical surface of the blood column, as well as by the media of the arterial wall. The outer surface of the media must contribute an important factor to the streak, as arteries have a wider, brighter streak than have veins of similar calibre.

An increase in thickness of the muscle coat and an increased index of refraction of the medial tissue, such as occurs in sclerosis, cause an increase in width and brightness of the arterial reflex. This produces the copper-wire artery, a burnished metallic appearance with a broader, softer reflex. Copper-wire arteries mean the commencement of thickening and hyaline degeneration of the media.

*Silver-Wire Arteries.* In the extreme form the vessel coat becomes opaque due to lipoidal infiltrates in the hyalinized media. The entire vessel reflects light homogeneously so that the whole thickness of the artery appears as a bright white reflex, like a wire of silver without any evidence of blood column.

The interpretation of slight changes must be done with caution, since the alterations are merely exaggerations of normal phenomena. The larger vessels near the disc may show unusual brightness in health. The changes are significant only when seen in smaller arteries.

*Vessel Walls.* The walls of the blood vessels, except those of the major branches on the optic disc, are normally invisible. Opacification of the vessel wall by fibrosis and lipoid infiltration may make the wall visible as a milky streak on either side of the blood column. This phenomenon is called parallel sheathing and is first evident at the arterio-venous crossing.

*Ophthalmoscopic Signs of Vascular Sclerosis*:—

1. Loss of translucency of vessel wall.
2. Alterations in the arterial light reflex: (a) Copper wire arteries. (b) Silver wire arteries.
3. Sheathing of vessels.
4. Arterio-venous crossing phenomena: (a) Constriction (apparent or real) of the veins. (b) Arterio-venous displacement.
5. Irregularity of the lumen—due to sub-endothelial degeneration.
6. Tortuosity and enlargement of the vessels.

*Types of Retinopathy*:—

1. Hypertensive retinopathy.
2. Renal retinopathy.
3. Pregnancy toxaemic retinopathy.
4. Diabetic retinopathy.

1. *Hypertensive Retinopathy.* The visible fundus changes are in the vessels and the retina.

1. The retinal vessels: (a) Spastic changes. (b) Sclerotic changes.

2. Secondary retinal changes: (a) Due to angiospasm. (b) Due to sclerosis.

1. *The Vascular Changes*: (a) *Spastic.* Spasm may be localized or general. The appearance of generalized spasm is described by Wagener in *The Kidney in Health and Disease*. They are:

i. Narrowing of calibre as seen with the ophthalmoscope. This is usually most marked in the arteries on the nasal side of the disc.

ii. Brightening of colour of the entire breadth of the arteries.

iii. Broadening and brightening of the reflex stripe.

iv. 'Nipping' of the veins at arterio-venous crossings or dulling of the venous colour near the crossing.

If the aetiological factor producing the tonic contraction of the vessel wall is removed, the blood pressure may come down to normal and the fundus resumes a normal apppearance. If hyperpiesia persists, changes occur in the vessel walls.

(b) *Sclerotic Changes.* These have been described earlier, e.g. marked localized difference in calibre, irregular tortuosity, well-developed copper-wire reflex, arterio-venous constriction and sheathing. As time goes on these increase in intensity: silver-wire arteries, gross sheathing and all the phenomena at the arterio-venous crossings.

2. *Secondary Retinal Changes*: (a) *The Angiospastic Changes*:—

i. The outstanding feature is retinal oedema. In localized spasm, vague patches of haze are seen in relation to the affected vessel. Generalized spasm leads to generalized

oedema with a cloud overlying the retina and some haziness of the nerve head.

ii. *Cotton-wool Patches.* These are soft, greyish-white, irregularly shaped patches lying in the superficial layers of the retina, with fluffy margins. They lie within oedematous areas, preferring the central region, particularly near the disc. If the general health improves they may disappear leaving no trace.

iii. *Haemorrhages.* These are linear or flame shaped if lying superficially, their shape being due to the configuration of the superficially placed nerve fibre layer of the retina. They may be round if lying more deeply beneath the nerve fibre layer.

(b) *The Arterio-Sclerotic Changes*: '*Exudates*'. Small discrete yellowish 'exudates' composed of lipoid degeneration products, always lying deeply underneath the vessels, are characteristic. They may be round or irregularly shaped, pin-point size up to half a disc in diameter. Most characteristically they are arranged in a star or fan-shaped manner at the macula. They indicate a more chronic process, oedema and cotton-wool patches indicating a more acute process, the former lasting for months, the latter for weeks.

*Signs at the Optic Disc.* In mild benign hypertension the disc is normal. In advanced disease, oedema occurs, its presence indicating a severe degree of vasoconstriction and sclerosis in the arterioles of heart, kidney and retina and other organs. Keith, Wagener and Kernohan distinguished 4 stages of so-called malignant hypertension, judging from the disc.

*Grade I.* Hyperaemia and mild oedema of the disc. Few haemorrhages and cotton-wool patches.

*Grade II.* More marked disc oedema. More haemorrhages, soft oedema patches. A few hard eudates.

*Grade III.* Recession of disc oedema. Macular star. Signs of arteriosclerosis.

*Grade IV.* Atrophy and pallor of disc. A few hard exudates. Few haemorrhages. Marked arteriosclerosis. Regressive changes tend to occur no matter what the general condition of the patient. Once Grade IV is reached, retinopathy does not recur as the atrophic retina does not respond a second time.

2. *Renal Retinopathy.* The fundus changes in primary glomerulo-nephritis are called renal retinopathy.

It is exceedingly difficult or impossible to distinguish classical renal retinopathy from malignant hypertensive retinopathy. Important if it occurs is the presence of secondary anaemia in chronic nephritis giving a pale optic disc in contrast to the red suffused one of advanced hypertension. Retinal oedema is more marked in nephritic cases, e.g., snow bank oedema round the disc, soft cotton wool patches scattered throughout the fundus pointing to the more intense vaso-spastic or toxic character of nephritis.

Marked sclerosis and hard discrete deposits point towards essential hypertension.

3. *Toxaemic Retinopathy.* The clinical course of the disease is divided into 3 stages.

1. The spastic stage.
2. The sclerotic stage.
3. The stage of retinopathy, when oedema and haemorrhages occur.

The first visible ocular sign of toxaemia is alteration of retinal arterioles.

Spasm passes gradually to sclerosis, to be followed by marked oedema and exudation, frequently resulting in a macular star, and may produce retinal detachment due to toxic oedema of the choroid. The picture resembles renal retinopathy.

4. *Diabetic Retinopathy.* Retinopathy in diabetes is not due to disease of arteries or arterioles, as the preceding group, but is due to disease of veins and venules. Ballantyne divides the stages of diabetic retinopathy into 5 types.

*Type 1.* Changes chiefly in the central area. Micro-aneurysms with or without punctate haemorrhages and exudates.

Micro-aneurysms may occur not uncommonly alone and it is difficult to distinguish them ophthalmoscopically from punctate haemorrhages. They are always strictly round and sharply defined because they are near the surface and sometimes possess a central reflex. They maintain their size over very long periods, for 3 or 4 years in some cases. They are histologically connected to the venules and lined by endothelium.

Punctate haemorrhages have no regular form, are less sharply defined because they are deeper and have a tendency to be absorbed. The discrete punctate exudates are the forerunners of the large irregular waxy patches. Some, however, are cicatricial remains of micro-aneurysms.

The vessels are normal, but histologically the venules are beginning to show change.

*Type 2.* 'Dot and Clot' haemorrhages. Confluent waxy exudates. The fundus now shows the textbook picture of diabetic retinopathy. The waxy exudates have a solid homogeneous appearance rather yellowish-white colour, distinguishing them from the grey, silvery-white granular patches of the hypertensive fundus.

*Type 3.* Changes in the vessels (veins) in the shape of new formed vessels, peri-phlebitis, phlebo-sclerosis and formation of knots, coils and loops in the distended veins.

Increasing haemorrhage in the retina and vitreous massive exudates.

Retinitis proliferans and detachment of the retina.

The striking series of changes in the veins may never occur or may occur fairly rapidly. Ophthalmoscopically they resemble extreme stasis in the venus system with attempts to form collateral channels, with knots, coils and leashes of new formed vessels, many of them into the vitreous (retinitis proliferans).

*Type 4.* Further advance of vessel changes. Increase in vitreous haemorrhages. Destruction of the retina. Thrombosis of retinal veins and haemorrhagic glaucoma.

This type comprises patients with blind eyes where the retinal condition is only seen histologically and reasures no comment.

*Type 5.* Mixed forms. At all ages from 30 onwards one sees fundi with diabetic changes (round haemorrhages, micro-aneurysms, waxy exudates, changes in the veins) as well as hypertensive changes (woolly exudates, striate or flame-shaped haemorrhages and changes in the arteries).

There is no relation between the severity of the diabetes the control of the condition by treatment and the presence or absence of retinal changes. Investigation along biochemical lines fails to discover any relation of diabetic retinopathy to blood cholesterol, blood urea and other factors.

There seems to be general consent that the duration of the diabetes is of greatest importance. Over 30% of patients have or will acquire pathological changes in the retina (not to mention cataract and other ocular manifestations of diabetes) in spite of the fact that they are rendered 'sugar free' and have a normal expectation of life.

## PASSING EVENTS

### ROBERT ROESLER DE VILLIERS FOUNDATION INCORPORATED

#### TO HELP CONQUER LEUKAEMIA

The Trustees of this Foundation have arranged a second competition inviting papers dealing with significant contributions to the knowledge of leukaemia and its effective treatment for which the prize-winner will receive an award of $1,000 to $1,500, according to the practical value of the paper submited.

The award will be further increased to $5,000 for a paper describing a cure or treatment which will keep the patient alive and enable him to live more or less normally, in much the same way as insulin does for the diabetic patient.

Those interested should communicate with the Secretary and Treasurer of the Foundation at 417 Park Avenue, New York 22, N.Y., U.S.A.

### SCIENTIFIC PAPERS FOR CONGRESS

The policy which has been adopted for the selection of papers for presentation to Congress is that the Organizing Committee has decided to invite papers on scientific topics from various members of the profession who are experts in their fields.

In addition, a limited number of papers are invited from those who wish to present them in the various sections.

Synopses of such papers must be in the hands of the Medical

Secretary not later than 3 March 1952. They should be addressed to:

W. Girdwood, Esq., F.R.C.S.,
Medical Secretary (1952 Medical Congress),
Medical House,
5 Esselen Street,
Hospital Hill, Johannesburg,

to whom any inquiries on this subject should be directed.

## IN MEMORIAM

### DR. W. A. CARDEN, M.R.C.S., L.R.C.P.

Dr. W. A. Carden died suddenly on 27 October 1951 in Johannesburg at the age of 79 years. He received his medical training at Guy's Hospital, London and married Miss Francis Green in 1899. She died on 3 August 1939. His daughter, Mrs. Eichstedt lives in Worcester, C.P. In 1943 he married again (Mrs. E. M. Cordell).

*Dr. W. A. Carden*

In 1899 Dr. Carden went to Korea as a medical practitioner where he spent 4 years with the English Church Mission. He came to South Africa in 1903 and begun to practise at Fraserburg, Cape. Five years later he went to Bothaville, O.F.S., where he was in practice for 22 years, including in his duties those of District Surgeon for several years.

From Bothaville he went to Worcester where he was for 12 years, retiring in 1942. He then settled at Deneysville where he lived to the time of his death.

Dr. Carden was a member of the Psychical Research Society. His passing will be mourned by many colleagues.

## REVIEWS OF BOOKS

### MALNUTRITION AND TIMES OF DISASTER

*Prevention and Treatment of Severe Malnutrition in Times of Disaster: World Health Organization Technical Report Series No. 45.* Report presented to the Fourth World Health Assembly. (Pp. 56. 2s. 9d.) Geneva: World Health Organization; Pretoria: Van Schaik's Bookstore (Pty.). 1951.

*Contents*: 1. Food Management. 2. Physiological, Clinical and Therapeutic Aspects. 3. Organizational Aspects. Bibliography.

A report on the prevention and treatment of severe malnutrition in times of disaster, prepared by a number of consultants and approved by the Joint FAO/WHO Expert Committee on Nutrition, is now available as No. 45 of the *World Health Organization: Technical Report Series*.

The problem is considered from three approaches: food management; the physiological, clinical, and therapeutic aspects of starvation; and the organization of relief programmes. A bibliography of recent works on the subject is appended to the report.

The general principles to be followed in drawing up plans for food management in emergencies are outlined. The most important steps to be taken as preliminary precautions before the emergency food shortage arises are the establishment of an authoritative central planning organization, the assessment of the total food requirements and production capacity of the population, and the accumulation of food reserves, especially of foods normally imported. The measures to be taken when the emergency arises should include: regulation of food procurement both at home and abroad; concentration of production on food of the highest possible calorie content; utilization of available foods to obtain the greatest nutritional advantage; and distribution of food by consumer rationing, combined with price control and food subsidies where necessary, to ensure equal shares.

The problem of starvation is then considered. While it is recognized that 'ideal' personnel, supplies and equipment for treatment are unlikely to be available in emergency conditions, an indication is given of basic requirements of personnel (auxiliary workers and specialists) and of equipment and facilities (heat, shelter, beds, toilets, cooking facilities, drinking water, disinfectants, soap, etc.).

In treating a starved individual primary account should be taken of the duration, variety and degree of the nutritional deficiency from which he is suffering. Classification criteria are given and the characteristics of starved persons are described. The report contains an outline of the treatment schedule to be followed, with indications of the caloric requirements of patients at various stages of starvation, the foods most suited to their diet, and of feeding programmes during the first few days, the first few weeks, and in subsequent months. It is encouraging to note that 'with proper treatment the great majority will probably recover and will regain substantial physical normality within a year'.

Specialized therapy is also examined. The most suitable calories and proteins for use in parenteral therapy—to be resorted to only when other methods of feeding are clearly inadequate or inapplicable—and suggested preparations for the clinical use of intravenous feeding are described. The special problems of infants and children are outlined, with reference to the characteristic signs of malnutrition and to the supplementary care required, particularly by the infant affected by diarrhoeal disease.

The organization of relief programmes in cases of large-scale and severe food shortage is to-day regarded as an international or world responsibility. Some indication is given of the kinds of relief teams needed and their work.

### NUTRITION

*Joint FAO : WHO Expert Committee on Nutrition: Report on the Second Session. World Health Organization Technical Report Series No. 44.* (Pp. 64. 3s.) Geneva: World Health Organization; Pretoria: Van Schaik's Bookstore (Pty.). 1951.

*Contents*: 1. Introduction. 2. Programmes of FAO and WHO. 3. Kwashiorkor. 4. Place of Applied Nutrition in Programmes for Promoting Economic and Social Progress. 5. Prevention and Treatment of Severe Malnutrition of Civilian Populations During War Periods. 6. Nutrition as a Subject in Medical Curricula. 7. Training in Nutrition in Underdeveloped Areas. 8. Nutritional Aspects of the Welfare of the Aged. 9. Nutrition and Degenerative Diseases. 10. Assessment of Nutritional Status. 11. Anthropometry applied to Nutrition.

The report on the second session of the Joint FAO : WHO Expert Committee on Nutrition is now available as No. 44 in the *World Health Organization: Technical Report Series*.

The nutrition activities of FAO and WHO in 1949 and 1950, and the programmes proposed for 1951 and 1952, are reviewed and the importance of continued co-ordination between the two Organizations, and of collaboration with non-governmental organizations, is stressed.

A survey on kwashiorkor in Africa, prepared by Prof. J. F. Brock and Dr. M. Autret (to be published in an English and a French edition as No. 8 in the *World Health Organization Monograph Series*), was studied by the committee. Recommendations relating to the prevention of this serious and widespread nutritional disorder, and suggestions for further investigation of the disease, are made in the report.

The place of applied nutrition in programmes for the promotion of economic and social progress is examined, and the development of nutrition demonstration projects, as a means of ensuring that improvements in health and well-being accompany improvements in economic and social conditions, is recommended.

Lack of personnel trained in nutrition is one of the chief obstacles to the development of nutrition programmes in underdeveloped areas. General indications about the types of personnel which should receive training, their instruction and the activities to be undertaken by them are given.

An interim guide to nutrition workers on the assessment of nutritional status is incorporated in the report. The different ways in which nutritional status may be assessed (from mortality—and morbidity—rates, from the growth of infants and children, from clinical appraisal of individuals, from dietary patterns and food consumption, and from laboratory tests) are described and the limitations of each indicated.

Other subjects discussed are: the necessity for including adequate nutrition instruction in the curricula of medical schools and public health courses; and a comprehensive report

on the prevention and treatment of severe malnutrition of civilian populations during war periods prepared by a group of consultants and published as No. 45 in the *World Health Organization: Technical Report Series*.

It is suggested that nutritional aspects of the welfare of the aged, the relationship between nutrition and degenerative diseases, and the problems involved in the development of anthopometric norms and standardized techniques of anthropometric measurements should be studied before the next session of the Committee.

### DORLAND'S MEDICAL DICTIONARY

*The American Illustrated Medical Dictionary*. By W. A. Newman Dorland, A.M., M.D., F.A.C.S. 22nd edition. (Pp. 1736 + xxvi, with 720 illustrations, including 48 plates. £4 17s. 9d.) Philadelphia and London: W. B. Saunders Company. 1951.

The 22nd edition of Dorland's *American Illustrated Medical Dictionary* celebrates the 50th anniversary of its first publication. On this occasion this remarkable book also takes on a new typography and design, which results in very much greater legibility, although it must be admitted that the legibility of previous editions did not leave very much to be desired.

As is to be expected, the revision which the re-setting has permited is very extensive, many old illustrations having been dropped and pertinent new ones included. This medical dictionary is one of the most remarkable achievements of our time and should be in the possession of every undergraduate and post-graduate medical reader.

For the medical writer it is a *sine qua non*.

### CECIL'S MEDICINE

*A Textbook of Medicine*. Edited by Russell L. Cecil, M.D., Sc.D. and Robert F. Loeb, M.D. Eighth Edition. (Pp. 1627 + xxxi, with illustrations. £5 10s. 6d.) Philadelphia and London: W. B. Saunders Company. 1951.

*Contents*: 1. The Infectious Diseases. 2. Diseases of Unproved Etiology. 3. Diseases of Allergy. 4. Diseases of Collagen. 5. Diseases Due to Physical Agents. 6. Diseases Due to Chemical Agents. 7. Deficiency Diseases. 8. Diseases of Metabolism. 9. Diseases of the Digestive System. 10. Diseases of the Respiratory System. 11. Diseases of the Kidneys. 12. Diseases of the Spleen and Reticulo-Endothelial System. 13. Diseases of the Blood. 14. Diseases of the Cardiovascular System. 15. Diseases of the Ductless Glands. 16. Diseases of the Locomotor System. 17. Diseases of the Nervous System. Appendix and Index.

With the publication of the eighth edition of Cecil's well-known *Textbook of Medicine*, Dr. Robert F. Loeb appears as co-editor. This volume is a mine of authoritative information which has been kept within the range suitable for the student and the general practitioner.

Important changes have been made and the Editors are to be congratulated on the remarkable achievement of shortening the book by 136 pages without losing important material. It is interesting to see that Infectious Mononucleosis has been moved into the section dealing with Viral Diseases. In the new (second edition) of the *British Encyclopaedia of Medical Practice* Sir Henry Tidy retains the old name of Glandular Fever and describes a classification of four types which apparently American authors find unconvincing.

It is important, however, that the serological reactions which have been regarded as establishing the diagnosis have been challenged.

No review of Cecil's *Textbook of Medicine* should omit drawing the reader's attention to the remarkable introduction to the section on Endocrinology by Prof. Fuller Albright, whose approach to endocrinology and, therefore, medicine, is a model which we may all with profit follow.

The eighth edition is assured of the excellent support which has always been given to its predecessors.

### OTORHINOLARYNGOLOGY 1950

*The 1950 Year Book of the Eye, Ear, Nose and Throat (November 1949–October 1950)*. The Eye, edited by D. Vail, M.D., D.Oph. (Oxon.), F.A.C.S. The Ear, Nose and Throat, edited by S. J. Crowe, M.D., with the collaboration of E. W. Hagens, M.D. (Pp. 446, with 138 figures. $5.00.) Chicago: The Year Book Publishers, Inc.

*Contents*: *The Eye*. 1. Ophthalmology, 1940-50. 2. The Eyelids and Lacrimal Apparatus. 3. The Orbit and Exophthalmos. 4. The Conjunctiva. 5. The Cornea. 6. The Iris and Ciliary Body. 7. The Lens and Cataract. 8. The Retina. 9. The Choroid. 10. The Optic Nerve. 11. Glaucoma. 12. Neurology and Visual Fields. 13. Refraction and Motility. 14. Surgery. 15. Therapy. 16. Miscellaneous.
*The Ear*. 17. Otolaryngology, 1940-50. 18. Hearing and Hearing Tests. 19. Otitis. 20. Otosclerosis and Fenestration. 21. The Inner Ear and Meniere's Syndrome. 22. Miscellaneous.
*The Nose and Throat*. 23. Nose and Sinuses. 24. Nasopharynx and Oropharynx. 25. The Larynx. 26. Trachea, Bronchi and Esophagus. 27. Miscellaneous.

The *Ear, Nose and Throat* section of this book starts with a special article discussing the age-old problem of removal of tonsils and adenoids, the regeneration of lymphoid tissue in the post-nasal space and its treatment by irradication. ACTH and Cortisone are also discussed in relation to oforhinolaryngology. Recent advances in audiology, otosclerosis and Meniere's disease are also concisely presented. The section on the trachea, bronchi and oesophagus, deals with new instruments for their examination and recent advances in their surgery.

From the ophthalmological standpoint, this small volume gives an adequate review of the world's ophthalmic literature for 1950. It is introduced by a special article which summarizes briefly the major advances which, concurrently with other branches in medicine, have occurred since 1940 and one cannot but be impressed by the amount of research work which has been undertaken throughout the war years and in the five years thereafter. Accepted theories of ocular physiology have been altered radically in the light of this work and important facts in the pathogenesis of glaucoma, to name but one condition, have been discovered. Therapy reviews include the use of ACTH, Aureomycin and alpha-tocopherol-acetate.

The main appeal of this section is to the busy practising ophthalmologist, rather than to the academician, and it is warmly recommended.

The articles in the 1950 *Year Book* are accompanied by references for those interested in consulting the original articles.

## CORRESPONDENCE

### SENSE, NONSENSE AND THE POLYSYLLABLE

*To the Editor*: I read Dr. M. Glass' letter in the *Journal* of 29 December with no pleasure at all. Each word of many syllables burst in my ears like a bomb. I think Dr. Glass believes that Dr. Freed is writing nonsense. Why not say so? Or is he trying to beat the poor man senseless with polysyllables?

May I also add a few words for Mrs. Annabelle Cohen? Dr. Freed, whom I do not know, and whose letter confused me, has had an idea which he has published in the form of a letter in the *Journal* which exists for that very purpose. This *Journal* is not specifically a scientific publication, although we are accustomed to read first-class papers in its columns. It is in this *Journal* published for all doctors in the country that we want to read letters about the crazy and half-baked ideas which bubble out of some of us. I feel sure that when Dr. Freed will wish to publish results in favour of his theories Mrs Cohen can look forward to reading a properly documented article. In the meanwhile her gibe about pen-and-paper investigators is not called for. She should hold her fire till she sees the whites of their eyes.

*Dazed Physician, Formerly Laboratory Worker.*

2 January 1952.

# The Medical Association of South Africa
# Die Mediese Vereniging van Suid-Afrika

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* * * *

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**(907)** Cape Town. Two rooms and share waiting room and services of nurse/receptionist. Urgent.

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## DURBAN

112 Medical Centre, Field Street. Telephone 24049

**PRACTICES FOR SALE**

**(D1)** In large coastal town suitable for a F.R.C.S. or M.R.C.O.G. Total gross receipts from June 1950 to June 1951, £4,995. Premium £3,100 includes drugs, fittings, surgery furniture and instruments. Terms could be arranged with reasonable cash deposit. Owing to ill-health owner wishes to sell immediately.

**(D5)** Twelve miles from Durban. Premium £450, including drugs. Cash preferred but terms will be accepted. Total gross receipts for period June 1950 to June 1951, £1,970. For immediate sale. Present owner setting up as a specialist in Durban.

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# Natal Provincial Administration

**VACANCY: FULL-TIME PHYSICIAN (PHYSIOTHERAPY) (CONTRACT): SALARY £1,500 PER ANNUM**

Applications are invited from suitably qualified candidates for appointment to the above post.

In addition to the above salary, a temporary cost-of-living allowance at present prescribed Public Service rates is also payable.

The successful applicant will be required to sign a contract for a period of 5 years.

Further particulars may be obtained from the Director, Provincial Medical and Health Services, P.O. Box 20, Pietermaritzburg, to whom all applications should be addressed to reach him on or before 15 February 1952. (AD 6762)

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## For Sale

Established physiotherapist's practice with good connections in new medical building in Johannesburg. Present owner wishes to retire due to health reasons. All equipment included in price of sale. Suite includes: reception room, consulting room, 2 treatment rooms with dressing cubicles, shower and steam baths, lavatory. Centrally heated, fitted Venetian blinds. Reasonable rental. Two practitioners could share. Principals only. Write to 'A. K. K.', P.O. Box 643, Cape Town.

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## Secretary Available

Medical secretary, 8 years' experience, including administration. English, aged 25. Requires post in a hospital or private practice. Address at present: The Cottage, Chesham, Bucks., England. Further details can be obtained on application from P.O. Box 458, Cape Town.

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## Physiotherapist Available

Physiotherapist. King's College Hospital. English. Aged 30. Eleven years' experience. Requires private or hospital post. Present address: 46 St. Ann Street, Salisbury, Wilts., England. For further particulars write to P.O. Box 458, Cape Town.

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## Therapist Available

Occupational therapist. Scottish Association. Aged 28. Seeks post with spastic or handicapped child, or hospital appointment. Present address: 36 Osbaldeston Gardens, Newcastle-on-Tyne 3, England. For further particulars write to P.O. Box 458, Cape Town.

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## For Sale

Examination couch, electric sterilizer, instrument trolley, medicine cabinet, 2-oz. dispensing scale, etc. Telephone Cape Town 7-3539, or write to 'A. K. L.', P.O. Box 643, Cape Town.

# Transvaal Provinsiale Administrasie

## VAKATURES BY PUBLIEKE HOSPITALE

Aansoeke word ingewag van kandidate met geskikte kwalifikasies vir die onderstaande poste by Publieke Hospitale in die Transvaal.

Aansoeke moet gerig word aan die Geneeskundige Superintendent of Verantwoordelike Geneesheer van die betrokke Hospitaal en moet volle besonderhede bevat aangaande die ouderdom, professionele, akademiese en taalkwalifikasies, ondervinding en huwelikstaat van die applikant en moet voorts 'n aanduiding bevat van die vroegste datum waarop diens aanvaar kan word.

| *Hospitaal* | *Vakature* | *Salaris* | *Aanmerkings* |
|---|---|---|---|
| *Barberton* | Deeltydse Mediese Praktisyn (1) | £680 per jaar | Moet 'n geregistreerde mediese praktisyn wees. Moet 4 sessies per week doen. |
| *Johannesburg Hospitaalbestuur en die Universiteit van die Witwatersrand* | Voltydse Assistent Chirurge (3) | £1,200x50–1,500 | Moet geregistreerde mediese praktisyns wees. Hoër kwalifikasies in snykunde 'n aanbeveling. Getroud plus (*a*) hieronder. Ongetroud plus (*b*) hieronder. |
| | Chirurgiese Registrateur (1) | £620–780–820–860 | Moet 'n geregistreerde mediese praktisyn vir 2 jaar wees. Getroud plus (*a*) hieronder. Ongetroud plus (*b*) hieronder. |
| | Voltydse Narkotiseurs (2) | £1,800 per jaar | Moet geregistreerde mediese praktisyn wees en moet behoorlik deur opleiding en ondervinding gekwalifiseerd wees. Getroud plus (*a*) hieronder. Ongetroud plus (*b*) hieronder. |
| | Voltydse Registrateur (Departement van Oor-, Neus- en Keelheelkunde) (1) | £620–780–820–860 | Moet 'n geregistreerde mediese praktisyn wees. Getroud plus (*a*) hieronder. Ongetroud plus (*b*) hieronder. |
| | Voltydse Registrateur (Departement van Urologie) (1) | £620–780–820–860 | Moet 'n geregistreerde mediese praktisyn vir 2 jaar wees. Getroud plus (*a*) hieronder. Ongetroud plus (*b*) hieronder. |
| *Pretoria* | Kliniese Assistent (Departement van Kindergeneeskunde) (1) | £620–780–820–860 | Moet 'n geregistreerde mediese praktisyn wees. Getroud plus (*a*) hieronder. Ongetroud plus (*b*) hieronder. |
| | Ongevallebeampte (1) | £620–780–820–860 | Moet 'n geregistreerde mediese praktisyn wees. Getroud plus (*a*) en (*c*) hieronder. Ongetroud plus (*b*) hieronder. |
| *Standerton* | Verantwoordelike Geneesheer (1) | £1,000x50–1,200 | Om Mediese en Administratiewe verantwoordelikhede oor te neem. Moet 'n geregistreerde mediese praktisyn wees. Getroud plus (*a*) hieronder. Ongetroud plus (*b*) hieronder. Plus £180 p.j. huistoelae. |
| *Verre Oos-rand, P.K. New State Areas* | Voltydse Spesialis Narkotiseur | £1,800 per jaar | Getroud plus (*a*) hieronder. Ongetroud plus (*b*) hieronder |

(*a*) £256 per jaar lewenskostetoelae.
(*b*) £80 per jaar lewenskostetoelae.
(*c*) £60 per jaar tydelike toelae.

Van persone wat aangestel word, sal verwag word om bevredigende sertifikate in te dien, asook om hulle te onderwerp aan 'n geneeskundige ondersoek by die betrokke hospitaal.

Aansoekvorms is verkrygbaar van die Provinsiale Sekretaris, Departement van Hospitaaldienste, Posbus 383, Pretoria.

Benewens jaarlikse salaris ontvang voltydse werknemers op die oomblik lewenskostetoelae, spoorwegkonsessie en word verlof toegestaan ooreenkomstig die hospitaal-verlofregulasies.

Die sluitingsdatum van aansoeke vir die poste is 11 Februarie 1952. (33424)

# South African Railways and Harbours Sick Fund

## APPOINTMENT OF ANAESTHETIST: EAST LONDON

Applications are invited from registered anaesthetists and medical practitioners with registrable qualifications for the position of anaesthetist, East London, at a salary of £878 per annum plus the fees and allowances prescribed by the Regulations of the Sick Fund and with the right of private practice.

The salary will be subject to adjustment in accordance with the census of members to be taken on 1 April of each year.

The appointment will be made in terms of the Regulations of the Fund and will be subject to termination on four months' notice being given by either side.

The successful applicant will be required to reside at East London, to take up the appointment on a date to be arranged, and to carry out his duties in accordance with the Regulations of the Fund.

Applications should reach the District Secretary, Cape Eastern District Sick Fund Board, 19 Terminus Street, East London, not later than 4 March 1952, and should state:—

1. Full name.
2. Qualifications (where and when obtained).
3. Experience (when and where obtained).
4. Date of birth.
5. Country of birth.
6. Married or single.
7. Whether fully bilingual.
8. Whether South African citizen.
9. What Government appointment, if any, is held.

Canvassing by or on behalf of any applicant is liable to disqualify such applicant.

Any further particulars required may be obtained from the District Secretary at the above address, on application.

P. J. Klem
*General Secretary*

Johannesburg
January 1952 (38)

## Siekefonds van die Suid-Afrikaanse Spoorweë en Hawens

**AANSTELLING VAN ALGEMENE CHIRURG, BLOEMFONTEIN**

Applikasies word van geregistreerde chirurge ingewag vir die betrekking van algemene chirurg, Bloemfontein, teen 'n salaris van £2,004 per jaar, plus gelde en toelaes wat in die regulasies van die Siekefonds voorgeskryf word, en met die reg om privaat te praktiseer.

Die salaris is onderhewig aan wysiging in ooreenstemming met die sensus van lede wat op 1 April van elke jaar afgeneem moet word.

Die aanstelling geskied kragtens die regulasies van die Siekefonds, en opsegging van dienste is onderworpe aan vier maande kennisgewing deur een van beide partye.

Die suksesvolle applikant moet in Bloemfontein woon, diens aanvaar op 'n datum wat gereël sal word, en sy pligte ooreenkomstig die regulasies van die Siekefonds uitvoer.

Aansoeke moet die Distriksekretaris, Distriksiekefondsraad, Oranje-Vrystaat, Charlesstraat 2, Bloemfontein, nie later nie as 1 Maart 1952 bereik, en applikante moet die volgende vermeld:

1. Volle naam.
2. Kwalifikasies (waar en wanneer verkry).
3. Ondervinding (waar en wanneer verkry en opgedoen).
4. Datum van geboorte.
5. Land van geboorte.
6. Getroud of ongetroud.
7. Of ten volle tweetalig.
8. Of Suid-Afrikaanse burger.
9. Watter staatsbetrekking, indien enige, beklee word.

Werwing deur of ten behoewe van enige applikant stel so 'n applikant bloot aan diskwalifikasie.

Enige verder besonderhede wat verlang word, kan op aanvraag van die Distriksekretaris by bovermelde adres verkry word.

P. J. Klem
*Hoofsekretaris*

Johannesburg
2 Februarie 1952

## Randfontein Estates Employees' Sick Benefit Fund

**MEDICAL OFFICER**

Applications are invited from registered medical practitioners for the post of Assistant Medical Officer to the above Fund to commence duties on 1 March 1952.

Applicant will be required to serve the members of the Fund in the prescribed area. Competency in anaesthetics will be a recommendation.

Salary £1,000 per annum. Private practice permitted. Applicants must reside in Randfontein, provide own accommodation, transport and telephone service.

Applications marked 'Medical Officer' stating qualifications and age, with supporting testimonials will be received by the undersigned up to noon on 19 February 1952.

Secretary's Office
Robinson Hospital
P.O. Box 37
Randfontein

F. A. Browne
*Secretary*

## Kromboom Nursing Home, Rondebosch, Cape Town

A newly built luxury nursing home in one acre of garden; large covered stoeps; mountain view. For all medical and convalescent cases. Resident doctor. Terms from 22s. 6d. a day. Telephone 6-6627; or P.O. Box 2829, Cape Town.

## Partner Required

Medical practitioner in established Transvaal country practice requires partner. Must be experienced in surgery and fully bilingual. Please furnish full details of experience and references in writing. For further particulars write to 'A. K. G.', P.O. Box 643, Cape Town.

## Vanderbijl Park Health Committee

**STAFF VACANCIES: PART-TIME MEDICAL OFFICER OF HEALTH AND PART-TIME CLINICAL MEDICAL OFFICER**

Applications are invited from bilingual qualified persons for the following positions in the Committee's service:

(a) Part-time Medical Officer of Health at a salary of £400 net per annum.

Applicants must be in possession of the Diploma in Public Health.

The successful applicant will be required to devote at least 10 hours per week to the Committee in addition to any time for the purpose of attending meetings of the Committee.

(b) Part-time Clinical Medical Officer at a salary of £400 net per annum.

The successful applicant will be required to carry out part-time clinical duties in the Committee's non-European Clinic, District N.W.2, and will have to devote at least 10 hours per week to these duties.

The successful applicants for both positions will be required to enter into contracts of service, to be approved by the Committee, which will embody the actual hours of duty and conditions of service.

Further particulars in connexion with the abovementioned positions may be obtained from the undersigned.

Applications, giving full details of qualifications, experience, age and the earliest date on which duties can be assumed, will be received by the undersigned up to noon on Monday, 18 February 1952.

Personal canvassing of Committee members for appointment in the gift of the Committee is strictly prohibited. Corroborated proof thereof shall disqualify a candidate for appointment.

P. R. Nell
*Secretary*

P.O. Box 3
Vanderbijl Park
16 January 1952
Notice No. 3/1952

## Vanderbijl Park Gesondheidskomitee

**PERSONEELVAKATURES: DEELTYDSE GENEESKUNDIGE GESONDHEIDSBEAMPTE EN DEELTYDSE KLINIESE GENEESKUNDIGE BEAMPTE**

Aansoeke word ingewag van bevoegde tweetalige persone om die volgende betrekkings in die Komitee se diens:

(a) Deeltydse Geneeskundige Gesondheidsbeampte teen 'n salaris van £400 netto per jaar.

Applikante moet die Diploma van Openbare Gesondheid besit.

Van die suksesvolle applikant sal vereis word om behalwe vergaderings van die Komitee wat hy bywoon, tenminste 10 uur per week aan die sake van die Komitee te wy.

(b) Deeltydse Kliniese Geneeskundige Beampte teen 'n salaris van £400 netto per jaar.

Van die suksesvolle applikant sal vereis word om deeltydse kliniese dienste in die Komitee se Nie-blanke Kliniek, Distrik N.W.2, te onderneem, en om tenminste 10 uur per week daaraan te wy.

Van die suksesvolle applikante om beide betrekkings sal verwag word om dienskontrakte wat deur die Komitee goedgekeur moet word, en wat die werklike diensure en diensvoorwaardes sal beliggaam, aan te gaan.

Nadere besonderhede in verband met bovermelde betrekkings kan van ondergetekende verkry word.

Aansoeke, waarin volle besonderhede van kwalifikasies, ondervinding, ouderdom en die vroegste datum van diensaanvaarding vermeld word, sal tot 12-uur Maandagmiddag, 18 Februarie 1952, deur ondergetekende ontvang word.

Niemand mag persoonlik invloed werf met die doel om aangestel te word nie; 'n kandidaat wat hom hieraan skuldig maak, kom nie vir die betrekking in aanmerking nie.

Posbus 3
Vanderbijl Park
16 Januarie 1952
Kennisgewing No. 3/1952

P. R. Nell
*Sekretaris*

Printed by Cape Times Ltd., Parow, and Published by the Proprietors, THE MEDICAL ASSOCIATION OF SOUTH AFRICA, MEDICAL HOUSE, 35 Wale Street, Cape Town. P.O. Box 643. Telephone 2-6177. Telegrams: 'Medical'


# TRUE STIMULANT THERAPY

✔ ACTHAR represents the natural stimulus for the adrenal glands to secrete the entire spectrum of cortical hormones at a rapidly increased rate. Thus the role of ACTHAR is to provide true stimulation therapy in a wide variety of diseases. ACTHAR neither substitutes nor replaces individual cortical hormones. Mobilization of physiologic mechanisms accounts for the safety of ACTHAR and permits prolonged courses of treatment without rest periods.

**ESTABLISHED INDICATIONS:** Rheumatoid arthritis, rheumatic fever, acute lupus erythematosus, severe asthma, drug sensitivities, contact dermatitis, most acute inflammatory diseases of the eye, acute pemphigus, exfoliative dermatitis, ulcerative colitis, acute gouty arthritis, secondary adrenal cortical hypofunction, acute alcoholism and acute delirium tremens.

ACTHAR is available in vials of 10, 25 and 40 I.U. (mg.). The Armour Standard of ACTHAR is now accepted as the International Unit; 1 International Unit is identical with 1 milligram of ACTHAR.

# ACTHAR

THE ARMOUR LABORATORIES BRAND OF ADRENOCORTICOTROPIC HORMONE (A.C.T.H.)

**THE ARMOUR LABORATORIES**

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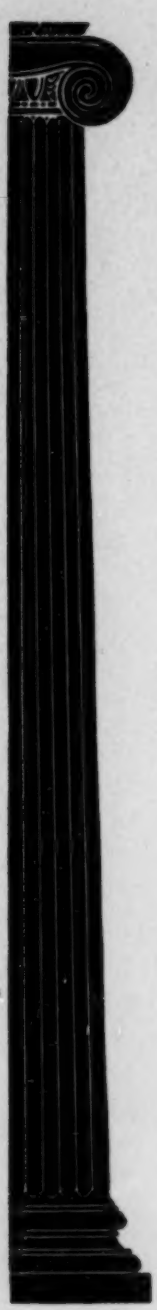

# SALICYLAMIDE
## (BENGER)

Recent intensive research indicates that in Salicylamide Benger (ortho-hydroxy benzamide) the clinician has a powerful weapon against pain—one that permits the massive doses not possible with other analgesics.

## ANALGESIC-ANTIPYRETIC ACTION

Hart. E. R. (1946) Bull. Fed. Ass. Soc. Exp. Bio. **5, 182,** has shown that Salicylamide possesses an analgesic potency 7½ times that of aspirin. This agrees with the clinical findings of Litter *et al.* (1951) J. Pharmacol, 101, 119 who treated 40 cases of rheumatoid arthritis, 17 of osteo-arthritis, 54 of fibrositis and 7 of rheumatic fever, and in half this group, the analgesic effect was described as "marked".

Salicylamide (Benger) is at least as effective as aspirin in reducing febrile conditions and its low toxicity enables the clinician to employ high therapeutic doses.

## ABSENCE OF TOXICITY

Numerous workers have demonstrated that the drug is well tolerated and in contra-distinction to salicylate therapy, prolonged and massive doses do not produce—

(1) gastric irritation
(2) renal damage
(3) changes in prothrombin times, or in erythrocyte and haemoglobin values.

REFERENCES:

(1) Seeberg, V.B. *et al* (1951) J. Pharmacol, 101, 275.
(2) Hofman H., Neubauer M. Deutsche Gesundheitwesen 5:776 June 1950.
(3) Euler. E., Remy R., Med. Klin. 45(37): 1,178, 1950.

## APPLICATION

Salicylamide (Benger) has no unpleasant taste and permits the use of high doses without undesirable side-effects. It may be used as a powerful general analgesic and in the treatment of rheumatic fever and other degenerative and inflammatory diseases of joints, muscles and ligaments. Reports of its use in various neuralgias are encouraging.

DOSAGE. The dose should be adjusted according to the patient's response (8–12 gms. per day have been used over prolonged periods without undesirable side-effects). The average effective adult dose is 2 gm. every four hours, night and day.

FURTHER INFORMATION WILL BE SUPPLIED BY:

**BRITISH CHEMICALS & BIOLOGICALS (S.A.) (PTY.) LIMITED.**

259 COMMISSIONER STREET, JOHANNESBURG.